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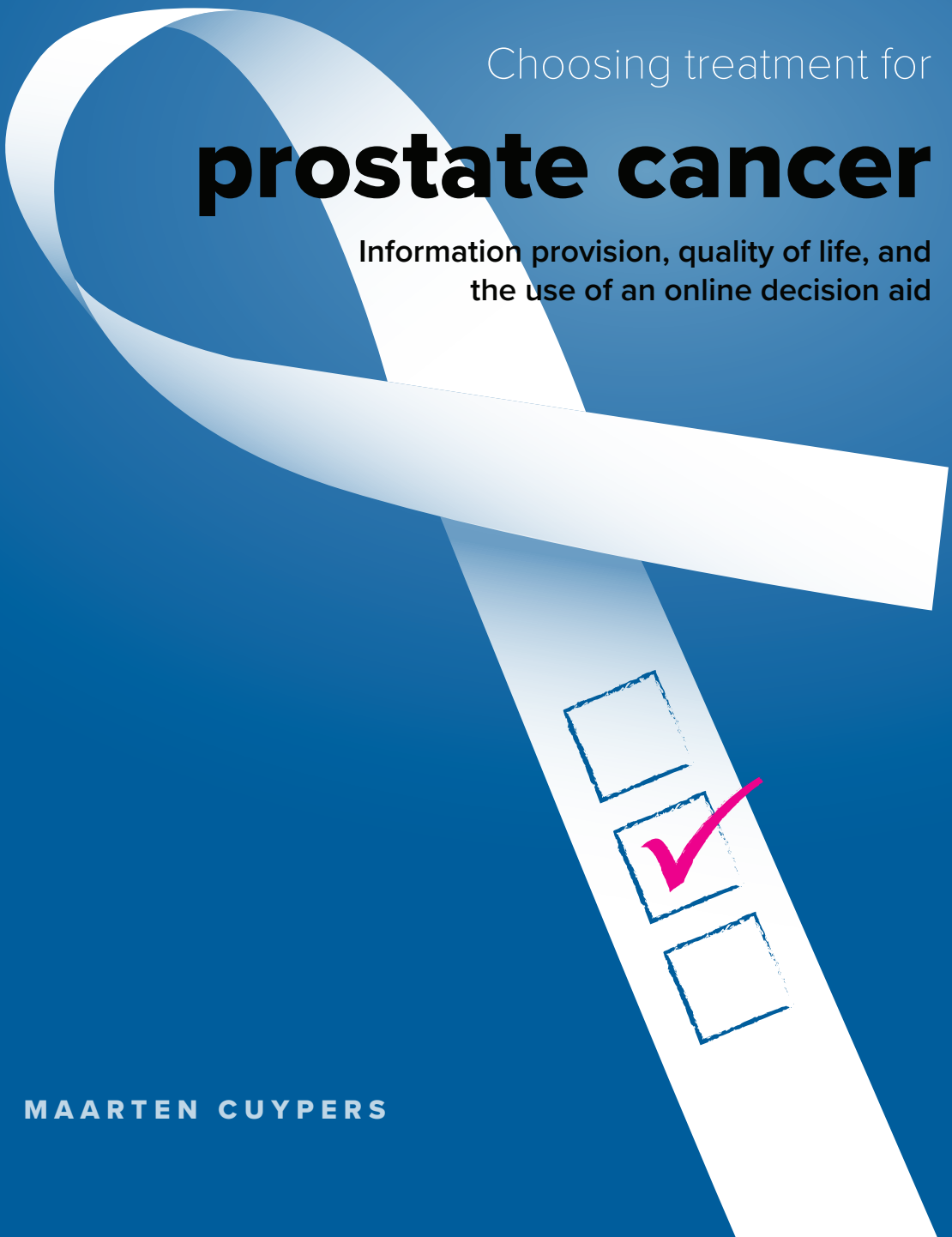

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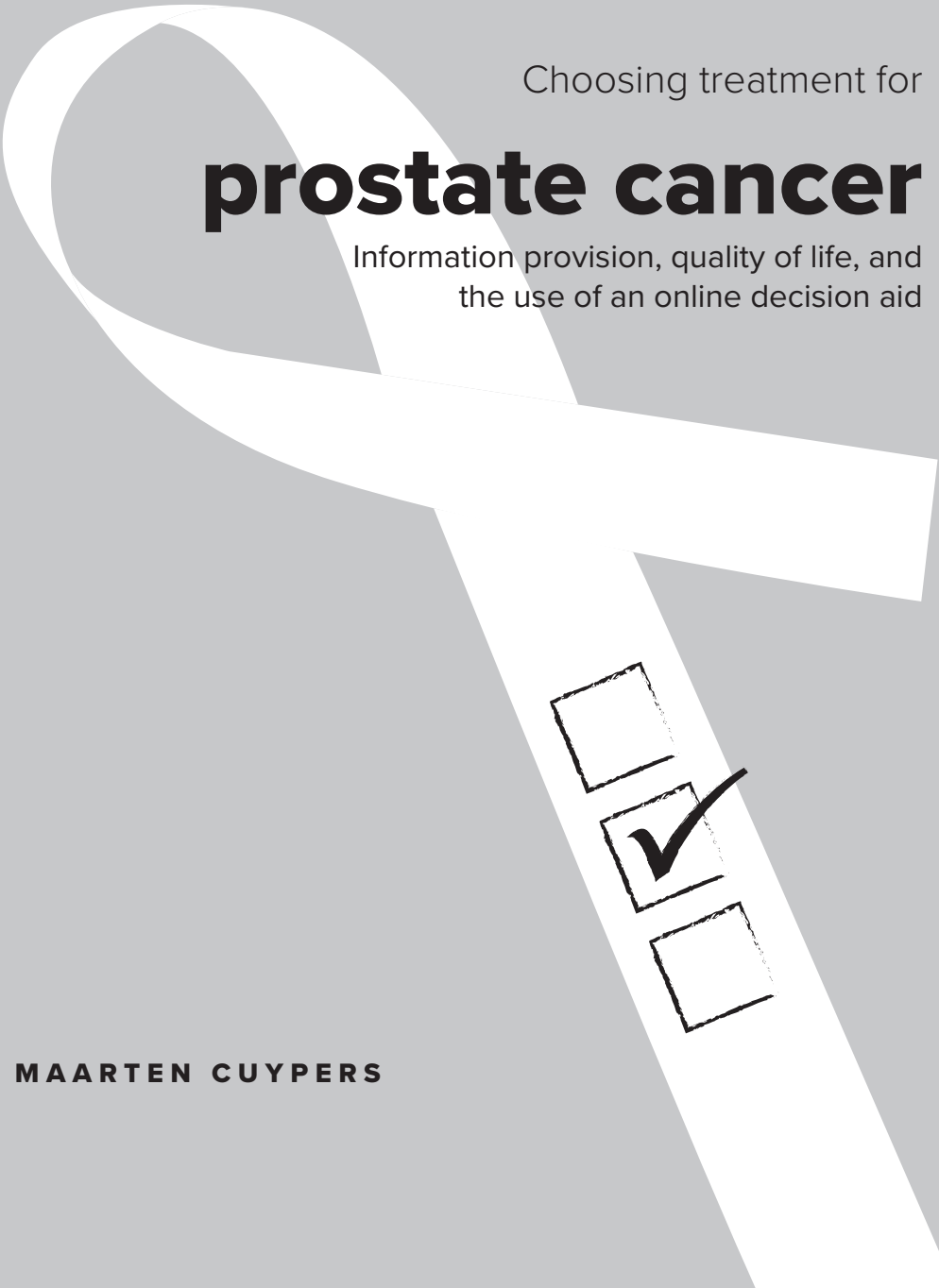

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P R O E F S C H R I F T

ter verkrijging van de graad van doctor aan Tilburg University
op gezag van de rector magnificus, prof.dr. E.H.L. Aarts,
in het openbaar te verdedigen ten overstaan van een door het college voor promoties
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door

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CONTENTS

Chapter 1

GENERAL INTRODUCTION

GENERAL INTRODUCTION

´If even the doctor does not know which treatment option would be best, how should I then decide what to choose? I am not a doctor, after all´. This could be the perception of a patient after receiving the diagnosis early-stage prostate cancer. In many cases, mild symptoms or an elevated PSA level in a (routine) blood test precede the diagnosis. Consequently, a man in a relative good health condition is suddenly confronted with a cancer diagnosis, which a patient may perceive as a serious and potentially life-threatening disease. Diagnosis can feel overwhelming at such a moment and choice awareness may be lacking. Explanation follows about the disease, its multiple treatment options, the different associated procedures and their potential benefits and side-effects and can cause patients to feel overloaded with information and to experience high levels of decisional conflict. This example highlights that providing high quality health care consists of more than diagnosing and treating a disease. In many medical situations, including early-stage prostate cancer, multiple appropriate treatment methods are available, as well as an option not to treat (immediately). In case of medically equivalent options, not only the medical content is relevant, but patient preferences and other personal circumstances determine which option provides the best patient-treatment fit. Optimal treatment choice is therefore dependent on shared doctor-patient decision making, consisting of discussion of all options, including the pros and cons so that the patient and doctor together come to a conclusion what would be the best option for this patient. However, this process of shared patient-doctor decision making, beyond the exchange of relevant medical information, is challenging.

First, evidence has shown that many patients are dissatisfied with the information they receive, patients sometimes lack choice awareness, or perceive discordance between the experienced and desired level of involvement in the decision process [1-6]. Moreover, health-care providers sometimes misinterpret patient preferences, which may result in treatment choices that are not concordant with patients values, and evidence also reveals that healthcare providers can be prone to overestimating the degree to which they already engage patients in a shared decision making process [7, 8]. To properly inform patients, enable them to take a more active role and to stimulate a joint patient-doctor decision process, patient decision aids (DA) can provide assistance in achieving shared decision making in routine clinical care [9, 10]. After exposure to a DA, patients report feeling better informed, are more knowledgeable, and more clear about their personal values [10].

At the start of the research project described in this dissertation, no patient DA including all active treatment options as well as the choice option not to start active treatment right away, was available and routinely used in care for prostate cancer patients in the Netherlands, even though prostate cancer is the most common cancer in man in the western world, including the Netherlands[11, 12]. The main goals of the project described in this dissertation were therefore: (1) Develop, (2) implement and (3) evaluate a DA for patients newly diagnosed with early-stage prostate cancer in everyday care in multiple healthcare centers in the Netherlands. For the purpose of improving national implementation, a consortium (JIPPA) was formed, consisting of three regional DA research groups that had each developed a DA for prostate cancer patients. Within the consortium, the same methods for patient evaluations and determining implementation rates were used, to facilitate comparison across the three studies.

To set the stage, the research described in this dissertation also presents (1) a retrospective analysis of decision roles and information satisfaction as reported by prostate cancer patients who are long after their initial treatment decision and who received care before the start of the JIPPA implementation project, as well as (2) an analysis of the change in patients´ self-reported health-related quality of life in the period before and after prostate cancer diagnosis, before treatment onset. The DA was tested within a cluster randomized trial. Novelty of this trial included a pragmatic approach, a long-term follow-up (12 months), and a detailed analysis of DA implementation and usage rates. The current chapter aims to describe the theoretical background and models underlying these studies.

Prostate cancer

Prostate cancer (Pca) is the most common cancer in men in the western world, and is diagnosed mostly in men between the ages of 50 and 70 [11, 12]. In the Netherlands, around 10,000 men are diagnosed with Pca every year (www.cijfersoverkanker.nl). In many patients, Pca is detected at an early stage [13]. At this stage, multiple medically equivalent treatment options are available [14]. Deciding between those options is challenging: a doctor can often not present a single superior option from a purely medical perspective, and patients are often not aware of differences between available treatments or their own preferences associated to these treatments [15, 16]. Careful treatment counseling is therefore required, which should at least include adequate information provision and elicitation of patient-preferences [9].

The prostate is part of the male reproductive system and is located below the urinary bladder and surrounds the urethra. The main function of the prostate is the production of prostate fluid for the transportation of semen [17]. Growth of the prostate starts

during puberty, regulated by hormones (testosterone). A healthy prostate has the size comparable to a walnut [18]. Men from 50 years and older frequently experience problems from growth of the prostate. Usually this is a benign enlargement of the prostate, which is not caused by cancer. With Pca, there is an uncontrolled growth of the prostate glandular cells. This changes the structure of the prostate gland, resulting in enlargement of the prostate and hardening of the prostate tissue [19].

In this dissertation, when the term Pca is used, we refer to prostate cancer at a localized stage. At this stage the cancer cells are located within the prostate (stage T1 or T2; Figure 1), without progression through the prostatic capsule and into surrounding tissue (T3) or other organs (T4) [20]. Pca progression during the localized stage is usually slow, and multiple, equally effective options can be considered for treatment, as well as the option not to treat immediately, as the tumor may not progress to an advanced stage at all [14].

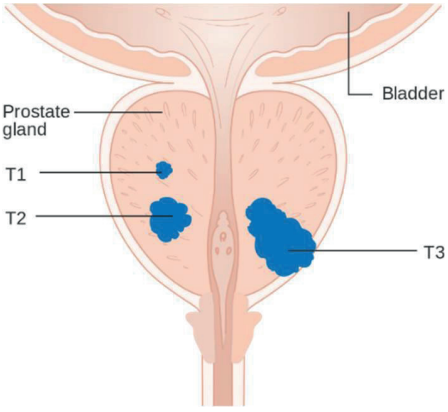

Figure 1. Location of the prostate and tumor stages.

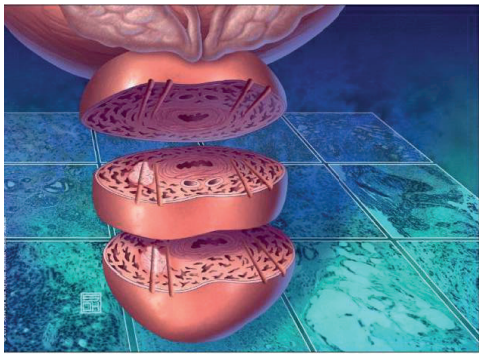

Figure 2. Three dimensional image of a prostate with cancer, after needle biopsy [21]

Growing number of Pca patients

In 1970, prostate specific antigen (PSA) was discovered as an indicator for Pca [22]. The level of PSA can easily be measured with a simple blood test. An elevated PSA level might be an indication for Pca and reason for further investigation, such as a rectal examination, imaging, and prostate biopsy (Figure 2). During the 1990's, PSA testing became common practice, and consequently, Pca detection has increased significantly [23]. As Pca mostly

develops at an older age, aging of our population, and the still increasing use of PSA testing contributes to an expected continued growth of Pca detection over the next decade [13, 24].

The probability of developing Pca at some point in life is estimated at just below 20%, while some studies showed that up to 50% of men between 70 and 80 years of age show some evidence of Pca [25]. However, most of these cancers will be non-aggressive and men will die of other causes without ever experiencing Pca symptoms [26]. Nevertheless, many men, when knowing that cancer is detected, feel the urgent need for treatment, even if the cancer might never develop symptoms and is unlikely to be fatal [27].

Preference-sensitive treatment options

The most endorsed curative treatment options for Pca (surgery, brachy therapy, and external radiotherapy) promise comparable chances on successful treatment and long-time survival [14]. However, each treatment has specific side-effects that can significantly impair a patient's quality of life (e.g. impotence, incontinence) [28-31]. These side-effects could even be perceived as worse than the cancer symptoms themselves. Alternatively, active surveillance can be a safe option for many men to postpone or avoid treatment without harming further survival perspectives. However, life then has to be continued with the knowledge of an untreated tumor being present [32, 33].

Without an obviously superior option, the best suiting treatment for an individual patient depends on various factors and is preference-sensitive [34]. First, clinical characteristics such as tumor size, co-morbidities and the physical condition of the patient, determine eligibility for one or more treatments. Second, personality characteristics and individual preferences determine which treatment the patient feels most comfortable with. For example, Patient A's fear for tumor progression may outweigh the perceived risk and burden of treatment side effects, resulting in a choice for surgery or radiotherapy. Patient B, on the other hand, might be reassured that active surveillance is as safe as immediate treatment, and chooses to postpone treatment and avoid the side effects associated to treatment. If patients' preferences would not be taken into account, and Patient A would be assigned to active surveillance, his daily life could be disturbed by anxiety about tumor progression, while if Patient B would have undergone surgery immediately and suffer from side effects, regret about the chosen treatment could impair quality of life to a greater extent in his case compared to a patient who accepted the risks of side effects as a consequence of immediate treatment upfront.

Medical decision making

Historically, most medical decisions were characterized by a strong focus on the disease itself -not the patient suffering from it- and the expertise of the doctor [35]. The more complex the disease or proposed treatment was, the more dominant the voice of the doctor was and, as a result, patients could feel excluded from this process. The exchange of information between a doctor and patient was often limited to the amount that was required to obtain a patient´s informed consent for undergoing treatment. Partly, this paternalistic model existed because many medical conditions only had a single treatment [36].

From the 1980´s onwards awareness increased that with advances in medical treatments, more complexity was introduced in deciding about which treatment would be best. For example, different treatments can have the same expected survival outcome, but may differ in the adverse treatment effects and risks involved. In such situations, a doctor can no longer solely rely on the medical characteristics to determine the best solution. Patient preferences and personal circumstances should then be evaluated to further guide the tradeoff between risks and benefits. Consequently, a more active patient role became necessary [35].

With increasing patient involvement, interest grew to deliver healthcare that is both effective and appropriate. Value-based healthcare was introduced as a term that aimed at optimal patient value while reducing health care costs [37]. An important driver in the development of value-based healthcare consisted of the observation of regional variation in treatments for the same disease. Routine clinical practice displayed wide treatment variations which could not be explained by illness severity or patient preferences alone 38. This variation has also been observed in Dutch Pca care [39]. Unwarranted regional variations in clinical practice for the same disease can be an indication for impaired healthcare quality. Care that is delivered does then possibly not reflect the latest scientific guidelines or patient preferences, but health-care provider preferences or financial incentives instead [40, 41]. Shared patient-doctor decisions may help to counter practice variation: When treatments reflect patient preferences, the same variation in treatments should be found across different regions or hospital locations [42, 43].

Shared decision making

Shared decision making (SDM) is a key concept throughout this dissertation. Definitions of SDM vary, but all include *'a balanced presentation of options and outcomes tailored to the individual patient's risk'* and '*active engagement with the patient to help clarify his own values and preference'* [44]. Active engagement does not necessarily mean that

the patient should always have an active role in evaluating options, information and decision-making, but it does require that the patient is aware that multiple options are available to him and that his personal values and preferences matter for selecting the most appropriate option. This ensures health care is centered around the patient, instead of focusing on the disease or treatment options [9].

Shared decision making (SDM) can help to achieve patient-centered care, as patients become more involved into their medical decision. SDM also contributes to the delivery of appropriate care. That is, when all available options are discussed, and patient values, preferences and circumstances are taken into account, it is more likely that the selected treatment is the optimal treatment for this particular patient, concordant with the individual patient's values and preferences and suiting his or her personal circumstances. This ensures that the inevitable scarce resources are allocated appropriately.

Benefits from SDM are found on multiple levels. First, there is an ethical imperative related to SDM, consisting of respecting patient autonomy [9]. Second, when being fully informed about all options and personal values have been taken into account, decision outcomes (e.g. chosen treatments) tend to be more conservative [45]. Consequently, SDM contributes to reduce over-treatment and possibly reduces (societal) health costs [46]. As such, SDM may also contribute to the sustainability of our healthcare system. Third, patient-reported outcomes after SDM include less decisional conflict, higher satisfaction with received care, less decisional regret, and better quality of life, although evidence for the latter two outcomes is less conclusive [47].

Procedures in SDM

Most SDM models can be translated into three steps towards a final treatment decision and start at the moment when it becomes clear that a decision has to be made [6, 9, 48]. A model that is brief and practical to translate to existing Pca care paths is the Three-talk model, with a Team, Option, and Decision talk [49]. The content of each step is summarized in Figure 3.

In Pca care, a multidisciplinary team (e.g., urologist, pathologist, radiologist, radiation oncologist, and oncology nurse) reviews all available evidence from previous tests and consents on what treatments can be considered according to the best available scientific evidence and relevant clinical guidelines. After the patient has received the Pca diagnosis, the aim of the Team talk is to explain all treatment options for which the patient is eligible and to provide additional information materials. Next, the aim of the Option talk is to weigh all benefits and risks from all options against personal patient preferences and values. An oncology nurse is often included in the Pca care

path to navigate patients through this step. Nurses often have more time available for counseling patients compared to doctors, and patients can perceive less of a power imbalance in conversation with a nurse [50]. After all options and patient values have been explored, the aim of the Decision talk is to make the treatment decision. Pca patients usually have this decision talk with their urologist.

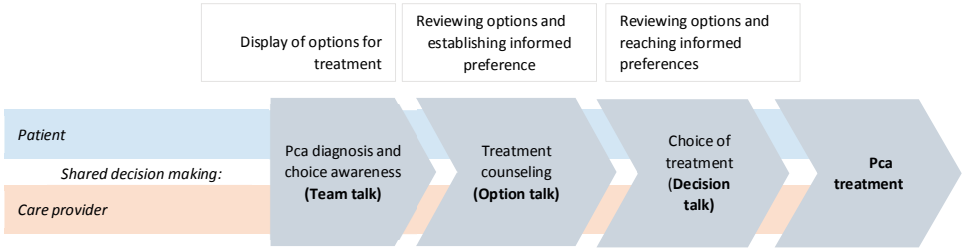

Figure 3. Three steps in SDM models, with the Three Talk model [49].

Decision aids

Even with stepwise models such as the Three Talk Model described above, it can be difficult for patients and doctors to initiate SDM and engage in a shared decision making process. Patients are often unaware that multiple options are available and that their preferences matter to select their personally optimal treatment option [51]. Doctors frequently misinterpret the desired level of patient involvement and overestimate the extent of SDM they already display [52-54].

To overcome these barriers in the execution of SDM, a variety of decision support interventions have been developed, of which decision aids (DAs) are the most comprehensive [55]. DAs come in multiple formats, ranging from concise paper leaflets to elaborate online tools. Regardless of their format, DAs provide balanced information about treatment options, with equal attention for the advantages and disadvantages of all options. DAs aim to help patients achieve an informed treatment preference. Some DAs therefore include implicit or explicit exercises to help patients to clarify personal values [9, 10, 56]. Quality criteria to guide DA development are provided by the International Patient Decision Aids Standards (IPDAS) collaboration [56, 57].

DA effects

A Cochrane review of the effects of DAs for various medical and screening decisions, including 105 RCTs, reveals that with a DA, patients are more knowledgeable, have more accurate expectations, and are more aware of what matters most to them [10]. In terms of quality of care, DAs help doctors and patients to talk more about really matters; not only what is medically possible, but also which goals the patient would like to achieve with treatment. In this way, a DA helps to lower decisional conflict, and establish a more valued patient-doctor relation. Increased satisfaction is often found for satisfaction with the choice, and the process of decision-making, including the preparation. However, satisfaction with the DA or overall information satisfaction has been studied less. Long-term studies into effects on regret are also rare. Overall, exposing patients to DAs does not seem to lead to adverse reactions, such as increased anxiety levels [10].

Implementation

Although many studies found beneficial DA effects, uptake of DAs in routine clinical care is still low, and existing Pca specific DAs vary in quality [10, 55, 58, 59]. Research on implementation of DAs in routine clinical practice, including Pca care, is also scarce [60]. Consequently, much of the current DA results are obtained within the setting of RCTs, which limit the external validity of these findings for daily routine practice [61, 62]. Moreover, many DA studies were single center studies, with small samples [10]. This supports the need for a more pragmatic approach with multiple study sites, to enhance structural implementation and gain a better understanding of the effects of decision aids in regular, everyday clinical practice. The research and implementation project described in this dissertation has been designed with those aims in mind, as described in more detail below.

Studies that did report DA implementation results have mostly been limited by a focus on the number of distributed DAs only [45, 63]. The relative reach within the patient population, or actual usage of the tool is therefore often unknown [45, 64]. Web-based DA dissemination provide opportunities to track usage, but usage can often not be linked to patient-reported outcomes (e.g. decision conflict, or DA evaluation). The studies reported in this dissertation aimed to provide a more structured approach to the evaluation of implementation by reporting about (1) reach within the eligible patient sample per hospital, about (2) actual usage in terms of usage of the different DA elements, and (3) linkage of usage to patient-reported outcomes and DA evaluations.

For dissemination of the DA in clinical routine we followed the Ottawa Hospital Research Institute (OHRI) Implementation Toolkit, which is based on the Knowledge to Action Framework [65-67]. The OHRI Toolkit describes five steps to implement DAs in clinical routine; 1. Identify the decision; 2. Find patient DAs; 3. Identify implementation barriers and explore ways to overcome them; 4. Implement DAs; 5. Monitor use and outcomes. In the research and implementation project presented in this dissertation, the decision that should be supported is the treatment choice in early-stage Pca (step 1). A suitable DA to be used within Dutch clinical care was developed as part of the current research project, building on a pre-existing, patient DA for Canadian patients with early-stage Pca (step 2). The third step from the OHRI Toolkit, concerns barriers (as well as facilitators) to DA use and SDM implementation. Important implementation barriers that are known from the literature[8, 50] include that patients do not feel knowledgeable enough and perceive a power imbalance in the patient-doctor relation. Doctors are insufficiently trained to initiate SDM and use DAs during clinical counseling, and often report time constraints to introduce and use DAs. Facilitators include that tools must not be disruptive of common routines, and easy to use [8, 50, 55]. To assess the extent to which the current DA was still prone to these barriers and facilitators, patients and care providers evaluated them in questionnaires as part of the studies included in this dissertation. Implementation of DAs (step 4), followed a pragmatic approach in the current study, by allowing hospitals to include the DA within existing information routines. The DAs web-based design allowed to track and link usage to reported outcomes (step 5).

Next to the number of DAs distributed, usage of the DA, and patient and care providers´ evaluations of barriers and facilitators, evaluation of implementation requires a broader approach. Besides the tool itself, and its users (patients and care providers), also the organization (e.g. hospital management) and external context (e.g. legislation, clinical guidelines) in which the DA is embedded, should be taken into account. Such a broad evaluation approach is provided by the Measurement Instrument for Determinants of Innovation (MIDI), which identifies barriers and facilitators at these four levels [68]. The first level consists of the innovation itself. In case of a DA this relates to aspects such as flawless functioning, and user-friendliness. The second level focuses on the user. With a DA, this relates to both the care provider who introduces the DA (e.g., received training), and the patient who actively engages with the tool (e.g., expectations prior to usage). At the third level is the hospital management that should provide sufficient resources (e.g. time, people, money) to work properly with the DA. Finally, the fourth level is the socio-political level to which the DA should comply. With the DA this relates to the content that should be consistent with relevant clinical guidelines and to the technical usage aspects which should comply with privacy legislations.

To investigate DA efficacy in a real world context, and to enable a thorough implementation analysis, the pragmatic cluster randomized trial reported in this dissertation was set up according to a hybrid effectiveness-implementation design, where simultaneous to testing the intervention, data was gathered on implementation [69]. In sum, the value of this dissertation lies in the pragmatic approach to contribute to the limited knowledge on implementing DAs in routine practice, while still being able to test the DA in a solid manner.

AIMS AND ORGANIZATION OF THIS DISSERTATION

The main objectives of the studies presented in this dissertation were:

- To assess the current state of information provision, and the impact of diagnosis and treatment decision-making in Pca care on patient-reported outcomes;
- To develop an online Dutch DA with values clarification exercises to support Pca treatment decision-making;
- To assess the impact of this online treatment DA on patient-reported outcomes and care providers' evaluations;
- To analyze implementation results of the current DA and two other novel Dutch Pca treatment DAs.

SDM requires an active patient role, and DAs can help patients in achieving such a role. The aim of **Chapter 2** was to investigate in a sample of Pca patients who already made a treatment decision in the past (average 48 months ago), what role preference they have, and how this role preference was associated with their satisfaction with the information that was received at the time of decision-making. To more closely investigate the impact of receiving a Pca diagnosis and the subsequent decision-making process, **Chapter 3** describes the changes in health-related quality of life (HRQoL) in the time between undergoing biopsy (pre-diagnosis) and making a decision about treatment in case Pca was detected. Furthermore, it was assessed if personality traits were associated with changes in HRQoL.

The development and pilot-testing of the DA that was developed is described in **Chapter 4**. The rationale and study design of the pragmatic, cluster randomized Prostate Cancer Patient Centered Care (PCPCC) trial are presented in **Chapter 5**. The aim of the PCPCC trial was to assess the impact of the DA on patient-reported outcomes, and care providers' opinions. Furthermore, uptake of the DA across hospital sites was studied.

The patient-reported outcomes are presented in two parts. First, **Chapter 6** presents effects of the DA on patient-reported decision process outcomes immediately after treatment decision-making, with decisional conflict as primary outcome measure, and knowledge and satisfaction as secondary outcomes. Satisfaction was assessed in terms of information satisfaction, and preparation for decision-making. Anxiety and depression symptoms were included as covariates, as they could potentially be affected by the DA, as well as have an effect on the other outcomes. Secondly, in **Chapter 7,** a 12-months follow-up is presented with the effects on decisional regret (primary), treatment satisfaction and information satisfaction (secondary) are presented. It was expected that undergoing treatment and experiencing potential side-effects could influence how patients in retrospect would evaluate the information that was received. Besides anxiety and depression, the patient-doctor relation was included as covariate. The aim of **Chapter 8** was to compare care providers' evaluations of DA counseling to standard information routines. Implementation and usage results of the DA are presented in **Chapter 9.**

Next to the DA studied in the previous chapters of this dissertation, two other Pca DAs were developed and tested simultaneous in The Netherlands. In **Chapter 10**, a joint evaluation of the implementation results is presented.

In **Chapter 11**, the main findings of this dissertation will be discussed, and the implications for future research and clinical practice are outlined.

A schematic overview of how the topics in this dissertation are related is presented in Figure 4.

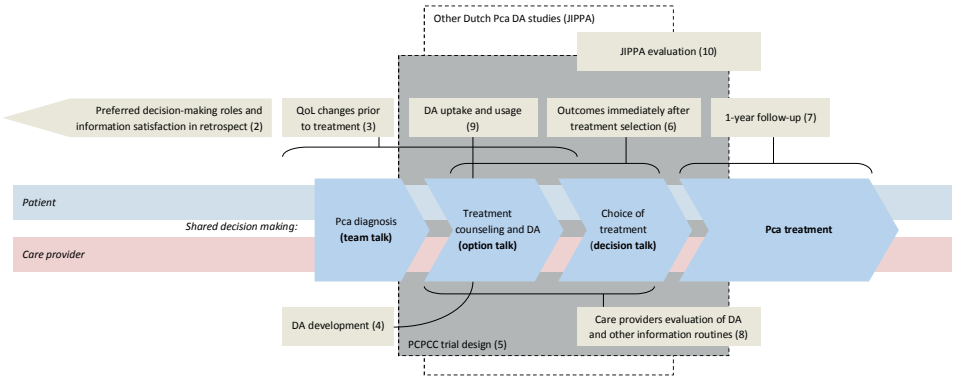

Figure 4. Schematic overview of the topics in this dissertation (chapter)

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Chapter 2

PROSTATE CANCER SURVIVORS WITH A PASSIVE ROLE PREFERENCE IN TREATMENT DECISION-MAKING ARE LESS SATISFIED WITH INFORMATION RECEIVED: RESULTS FROM THE PROFILES REGISTRY

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ABSTRACT

Objective - To investigate decision-making role preferences and their association with the evaluation of information received in a sample of low and intermediate risk prostate cancer (Pca) survivors.

Methods - Cross-sectional study involving 562 men diagnosed with low or intermediate risk Pca (median time since diagnosis of 48 months), measuring preferred decision-making role (Control Preference Scale) and the evaluation of information received (EORTC QLQ-INFO25). Analyses were performed using ANOVA, chi-square tests and multivariable linear regression models.

Results - Men who preferred a passive role were older and less educated than other preference groups and more often selected a non-invasive treatment option (all with $p<.001$). The passive role preference group reported having received less information, judged the received information as less helpful and indicated lower overall satisfaction with information received (all with $p<.05$). Role preference groups did not differ in their desire to receive more information.

Conclusion - Compared to non-passive preference groups, the preference for a passive role in Pca treatment decision-making is associated with less satisfaction with information received.

Practice implications - Assessment of role preferences and tailored information-provision could improve satisfaction with information received and perhaps may ultimately lead to improved patient participation in treatment decision making.

1. INTRODUCTION

Shared decision-making (SDM) is widely recognized as best practice in preference-sensitive treatment decision-making [1-3]. Following the principles of SDM, a clinician shares the best available evidence on the treatment alternatives and the patient receives support in sharing his personal values and preferences [4]. Across several medical conditions it has been found that a large majority of patients (75%) prefers this collaborative or even a more active role, though leaving a substantial proportion of patients (25%) preferring a passive role in treatment decision-making [5]. Some studies with SDM interventions such as decision support tools show improved patient involvement, while other studies show little variability over time, indicating that role preferences could represent an intrinsic personality trait that is consistent over time and situations [1, 6]. Although patients prefer different roles for involvement in treatment decision-making, information provision practices are often standardized for all patients. Whereas the variation in decision-making role preferences has been studied before, its relation with the evaluation of information received has so far remained untested [3, 5, 7, 8].

The present study aims to investigate the association between decision-making role preferences and the evaluation of information received in a sample of low and intermediate risk (stage cT1 and cT2) prostate cancer (Pca) patients. Incidence of low and intermediate risk Pca is growing due to an aging population and increased use of PSA screening [9-11]. Available treatments for low and intermediate risk Pca offer oncologically equivalent outcomes, but come with different treatment side-effects that could have a significant impact on quality of life, emphasizing the need for proper information provision and careful determination of patients' preferences and characteristics [12, 13]. However, it was found that one in three Pca patients is dissatisfied with information received [14]. Our hypothesis is that patients with a passive role preference require less information than patients with a preference for an active decision-making role. However, for satisfaction with information received we hypothesize that patients with a passive role preference are equally satisfied with information received as they prefer to delegate the final decision in a larger extent to the clinician involved and may have a lower need for information.

2. METHODS

2.1 Participants and data collection

Seven hospitals in the southern area of the Netherlands Cancer Registry (NCR) participated in this study. Per hospital a random selection was made of 150 Pca patients who were diagnosed between 2006 and 2009 (stage cT1-cT3). Patients with a cT3-stage tumor were later excluded from this sample as their treatment alternatives and medical condition are less comparable to the cT1 and cT2 stage. Data was collected in October 2011 within Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship (PROFILES). PROFILES is a registry for the study of the physical and psychosocial influence of cancer and its treatment from a dynamic, growing population-based cohort of both short- and long-term cancer survivors. PROFILES contains a large web-based component and is linked directly to clinical data from the NCR [15]. Urologists sent their (former) patients a letter to inform them about the study and to invite them to complete an online questionnaire. On request, patients received a paper questionnaire that could be returned in a pre-stamped envelope. Patients consented on linking questionnaire data to their clinical data from the NCR. Earlier studies on related topics have been carried out within in the same sample [14, 16]. Our study protocol was reviewed and centrally approved for all participating hospitals by the medical ethics committee of one of the participating hospitals.

2.2 Measures

2.2.1 Socio-demographic and clinical characteristics

Clinical and patient information was obtained from the NCR (i.e., date of birth, date of diagnosis, disease stage, and initial treatment). The questionnaire included questions on socio-demographic variables (i.e., marital status, employment status, and educational level).

2.2.2 Preferred decision-making role

The Control Preferences Scale (CPS) was used to assess the role a patient prefers in treatment decision-making [17]. Responses to this single item question range on a unidimensional scale from passive ('I prefer to leave all decisions regarding treatment to my doctor') to active ('I prefer to make the decision about which treatment I will receive'). The five answer categories are condensed into three categories, with the first two roles combined as passive, the middle role as shared decision-making (collaborative), and the last two roles as a preference for an active role. The CPS has been used to measure role preferences worldwide for multiple medical conditions and proven to be a valid and reliable measure [18-20].

2.2.4 Evaluation of information received

The evaluation of information received was assessed with the EORTC QLQ-INFO25 questionnaire [21]. The EORTC QLQ-INFO25 consists of four subscales which assess the perceived receipt of information about (i) the disease; (ii) medical tests; (iii) treatment, and (iv) other care services. Additionally, eight single items assess the receipt of information in different formats (e.g. written information, information on CDs or tape/ video), evaluation of the amount of information and satisfaction with the amount and helpfulness of information. All responses were given on a four-point Likert scale (1- not at all, 2-a little, 3-quite a bit, 4-very much), except for four single items that have a binary yes/no scale. Subscales were converted to a 0-100 outcome. Reliability of the full scale (α >.91) was excellent, subscale reliability (range between α=.74 and α =.89) was acceptable to good.

2.2.5 Health-related Quality of Life

We used a general measure for health-related quality of life (HRQoL) in cancer patients (EORTC QLQ C30) and supplemented this with a Pca specific module (EORTC QLQ PR25) [22, 23]. Both scales were used to assess functional outcomes and symptom burden, as a previous study reported a negative correlation between HRQol and satisfaction with information received [14]. All responses were given on a four-point Likert scale (1- not at all, 2-a little, 3-quite a bit, 4-very much), except for two single items evaluating Global health on a seven-point scale. Subscales were converted to a 0-100 outcome. Reliability of the full C30 was excellent (α >.92), for the full PR25 scale reliability was good (α >.77), subscale reliability (range between α=.63 and α =.91) was good. Three symptom scales (Nausea, Bowel, Hormonal) and one functional scale (Sexual functioning) were excluded for further analysis because of poor internal consistency (α <.60)

2.3 Statistical analyses

Patient and tumor characteristics were compared between decision-making role preference groups by using analyses of variance (ANOVAs) for continuous variables and chi-square analyses for categorical variables. Mean scores on the EORTC-QLQ-INFO25 and HRQoL-scales for different decision-making role preference groups were compared using ANOVA and LSD post hoc-tests or chi-square analyses for dichotomous items. Independent sample t-tests were conducted to investigate potential differences in satisfaction with information received between the two tumor stage groups (cT1 and cT2). For all EORTC-INFO-25 subscales linear regression analyses were carried out to investigate the association of these scales with decision-making role preference groups, controlling for age and educational level as being previously identified variables associated with role preferences [5]. As we assumed, received information could be

different depending on the selected treatment, linear regression analyses were repeated per treatment group (active surveillance, surgery, radiotherapy). Multicollinearity was checked in all relevant analyses. All analyses were performed using SPSS version 20.0 (Statistical Package for Social Sciences, Chicago, IL, USA). *P*-values <.05 were considered statistically significant.

3. RESULTS

The questionnaire was completed by 562 participants (71%). Non-responders were older than responders (mean 68.9 vs. 66.5, $p<.001$), men with unverifiable addresses did not differ in age compared to responders. Also, no group differences were found in tumor stage between respondents, non-respondents and patients with unverifiable addresses ($p=.306$). Questionnaires were filled in with a median of 48 months since diagnosis. Time since diagnosis was not correlated to decision-making role preferences, ($r(612) = .059$, $p= .141$.

3.1 Univariate results

Fifty-nine percent of the responders preferred a collaborative decision-making (CDM) role, whereas 19% preferred a passive (PDM) role and 22% preferred an active (ADM) role. Men with a preference for a PDM role were on average older, had lower education levels and more often had a lower socio-economic status (SES), compared to men with a CDM or ADM role preference (Table 1).

Men with a preference for an ADM role had more often received surgery or brachytherapy as initial treatment, while men with a preference for a PDM role had more often received active surveillance or external radiation therapy ($p<.001$). Role preferences were not related to clinical characteristics (tumor stage and Gleason score) or marital status (Table 1).

Table 1. Demographic and clinical characteristics

	Preferred decision-making role			
	Passive N (%)	**Collaborative N (%)**	**Active N (%)**	***p* value**
All	100 (19)	320 (59)	118 (22)	
Age at diagnosis, mean (SD)	68.5 (7.1)	66.5 (7.0)	64.0 (7.4)	<0.001
<55	4 (4)	21 (7)	10 (8)	
56-65	34 (34)	114 (36)	66 (56)	
66-75	44 (44)	155 (48)	34 (29)	
76>	18 (18)	30 (9)	8 (7)	
Marital status				0.722
Married/living together	85 (86)	272 (86)	104 (89)	
Other	14 (14)	44 (14)	13 (11)	
Education				<0.001
Primary education	21 (21)	45 (14)	13 (11)	
Secondary education	27 (27)	77 (25)	22 (19)	
Intermediate education	36 (37)	121 (38)	34 (29)	
Bachelor or master degree	15 (15)	73 (23)	48 (41)	
Socio economic status (SES)				0.018
Low	15 (15)	53 (17)	15 (13)	
Medium	43 (43)	126 (40)	31 (27)	
High	37 (37)	129 (41)	66 (58)	
Institutionalized	5 (5)	6 (2)	2 (2)	
Pathological T category				0.176
cT1	65 (65)	184 (58)	62 (53)	
cT2	35 (35)	136 (43)	56 (47)	
Gleason score				0.272
2-6	58 (60)	187 (60)	74 (65)	
7	29 (30)	77 (25)	30 (26)	
8-10	9 (10)	48 (15)	10 (9)	
Initial treatment (obtained from NCR[1])				<0.001
Radical prostatectomy	20 (20)	81 (25)	42 (36)	
Brachytherapy	4 (4)	53 (17)	25 (21)	
External beam radiotherapy	17 (17)	30 (9)	7 (6)	
Surveillance	28 (28)	65 (20)	24 (20)	
Hormone therapy	12 (12)	43 (13)	8 (7)	
Other	19 (19)	48 (15)	12 (10)	
Satisfaction with information provision				0.002
Dissatisfied	46 (48)	92 (29)	33 (28)	
Satisfied	50 (52)	222 (71)	83 (72)	

[1] Netherlands Cancer Registry

Men with a preference for a PDM role reported having received less information, having perceived this information as less helpful, and reported lower satisfaction with information received. Across preferred decision-making roles there was no statistically significant difference in the desire for more or less information (Table 2). Effect sizes when comparing all three groups were small (table 2) [24]. When directly comparing PDM and ADM role preference groups, effect sizes range from d=.32 to d=.56, indicating a medium effect size [24]. Time since diagnosis was not correlated to satisfaction with information received or any of the EORTC-INFO-25 subscales (all with $p>.05$). Five of the 17 analyzed HRQoL subscales showed a statistically significant difference across decision-making role preferences (table 2). Most relevant differences were found on Physical functioning, which was lower for men with a PDM role preference and sexual activity, which was higher for men with an ADM role preference (all with $p<.05$).

As the cT1 and cT2 tumor stages were equally distributed among the subgroups we decided to combine both tumor stages in further analyses.

3.2 Multivariable linear regression

Controlled for age, education, physical functioning and sexual activity, the preference for a PDM role was associated with more negative evaluations of the amount of information provided on specific content (medical tests, treatments and other services), the overall amount of received written information, and the helpfulness and satisfaction of the received information (Table 3). To test the assumption if specific treatments affected outcomes, analyses were also conducted per treatment group. This did not yield treatment specific outcomes (data not shown). Moreover, no hospital specific effects were found on the distribution of decision-making role preferences or the evaluation of information received (data not shown).

Table 2. EORTC-INFO-25, QLQ-C30 and PR25 scales means (± SD)

	Preferred decision-making role				
EORTC-INFO-25	**Passive**	**Collaborative**	**Active**	***p* value**	**η^2**
Information about the disease	50.1 (21.3)*	55.6 (22.2)	56.9 (21.6)	0.060	
Information about medical tests	53.9 (28.3)*	64.4 (27.4)	66.2 (30.6)	**0.003**	0.02
Information about treatments	44.9 (29.7)**	56.5 (25.4)	60.5 (26.5)	**0.000**	0.04
Information about other services	14.5 (19.8)*	21.4 (25.7)	22.0 (27.1)	**0.045**	0.01
Information about other places of care	15.8 (28.5)	21.0 (31.5)	18.1 (30.1)	0.301	
Information about things you can do to help yourself	19.4 (28.9)	25.1 (31.1)	24.3 (31.0)	0.283	
Written information	63.5 (48.4)**	80.5 (39.7)	83.1 (37.7)	**0.001**	0.03
Information on CD/audio/video	3.1 (17.4)	4.7 (21.3)	10.2 (30.4)*	**0.045**	0.01
Satisfaction with information received	52.8 (26.3)*	62.4 (27.4)	62.4 (28.0)	**0.008**	0.02
Helpfulness of information received	56.8 (27.0)*	67.4 (25.0)	67.3 (26.3)	**0.002**	0.02
Want more information (%)	26.5%	24.4%	29.7%	0.529	
Want less information (%)	3.1%	2.3%	3.4%	0.761	
EORTC-QLQ-C30					
Global Health	76.8 (17.8)*	78.0 (17.0)	81.5 (17.1)	0.089	
Physical functioning	81.4 (18.1)*	85.1 (17.6)	88.3 (17.5)	**0.017**	0.02
Role functioning	80.7 (27.5)	82.9 (24.7)	86.5 (22.2)	0.219	
Emotional functioning	87.0 (17.9)	88.1 (17.7)	90.6 (16.0)	0.277	
Cognitive functioning	83.3 (19.4)	84.9 (20.0)	87.1 (18.5)	0.349	
Social functioning	89.5 (20.5)	90.5 (18.9)	91.1 (16.0)	0.808	
Fatigue	19.6 (21.4)	19.5 (21.6)	14.2 (18.4)*	0.053	
Pain	14.8 (22.8)	14.1 (22.7)	13.8 (23.0)	0.945	
Dyspnoea	20.4 (27.8)*	14.1 (24.6)*	11.3 (20.5)*	**0.021**	0.01
Insomnia	21.3 (30.9)	18.0 (26.9)	14.1 (23.2)*	0.141	
Appetite	3.7 (13.3)	3.7 (13.4)	.6 (4.3)*	**0.046**	0.01
Constipation	6.0 (14.6)	5.9 (17.4)	6.3 (17.0)	0.978	
Diarrhoea	7.3 (19.5)	4.7 (14.1)	3.7 (12.9)	0.193	
Financial	2.4 (8.7)	5.1 (13.4)*	2.3 (9.5)	**0.033**	0.01
EORTC-QLQ-PR25					
Sexual activity	23.6 (21.2)	26.9 (22.5)	32.6 (23.9)*	**0.011**	0.02
Urinary	20.7 (15.2)	18.5 (14.3)	17.7 (14.4)	0.292	
Incontinence	18.4 (30.3)	14.8 (23.8)	15.9 (25.8)	0.796	

* $p<0.05$ in post hoc LSD-test
** $p<0.001$ in post hoc LSD-test

Table 3. Standardized betas of multivariable linear regression analyses evaluating the association of independent variables with the EORTC QLQ-INFO25 scales, all patients combined

	Information about					Amount of				
	the disease N=519	**medical tests N=526**	**treat-ments N=508**	**other services N=510**	**other places N=533**	**things to do N=531**	**written infor-mation N=542**	**CD/ audio/ video N=540**	**Satis-faction N=532**	**Help-fulness N=521**
Age	-.029	.005	-.164**	-.167**	-.055	-.122*	-.167**	-.037	-.013	-.026
Education	.105*	.159**	.093	.045	.057	.001	.078	-.054	.061	.108*
Physical functioning	.058	-.006	.027	0.063	.086	.039	.003	.059	.119*	.079
Sexual activity	-.046	-.001	-.096	-.084	-.022	-.082	.013	.059	-.085	-.102*
Passive vs. collaborative	-.058	-.112*	-.166**	-.098*	-.041	-.076	-.134*	-.037	-.111*	-.134*
Active vs. collaborative	.044	.027	.043	-.028	-.059	-.012	-.011	.057	-.009	-.005

* $p<.05$
** $p<.001$

4. DISCUSSION AND CONCLUSION

This study showed that decision-making role preferences are associated with the perceived amount of information, helpfulness and satisfaction with information received. Men with a PDM role preference indicated having received less information, found it less helpful and were less satisfied with the information received. Despite this more negative evaluation, men with a PDM role preference did not differ from the ADM and CDM preference groups in their desire to have received more information. Functional outcomes and symptom burden could not explain the differences between decision-making role preferences.

Previous reports that age and education are related to decision-making role preferences were confirmed in our study [5]. Overall, younger and higher educated men more often preferred an ADM role. A PDM role preference was found more often across older and less educated men. Although the response rate in our study was quite good and similar to comparable studies from the PROFILES registry [25, 26], we observed that non-responders in our study were slightly older compared to responders. It should therefore be taken in consideration that the proportion of men preferring a PDM role is slightly under represented in our sample. It is therefore expected that less non-responders would have further strengthened our findings.

Our finding that men with a PDM role preference were generally more negative about information received is surprising as it would be expected from this group to rely less on information provided. Although one in four men with a PDM role preference indicated a desire to have received more information, this is comparable to what was found in men with a preference for an ADM or a CDM role. An earlier study in Pca patients on the information needs of the different decision-making role groups found that different role preference groups require information about the same topics [27]. However, there is also evidence that some patients rely to a greater extent to personal factors –like the opinion and experience of others- than only the information provided when making a treatment decision [28]. It could therefore be that it is not the content or amount of the provided information that is most troublesome for men with a preference for PDM, but that the provided information is not what they primarily need to base their decision on.

A previous study on the relation between HRQoL and satisfaction with information received in a similar sample indicated an association between functional outcomes, symptom burden and the evaluation of information received [14]. In the current study these HRQoL outcomes were not able to explain the differences between role preference

groups on the information scales. This could indicate HRQoL and decision-making role preferences both explain separate areas of the variation within the information scales. To investigate this causality, a prospective study on this topic is needed.

To improve information provision practices to men with a preference for a PDM role, early recognition of role preferences may be needed. Although we found age and education level to be associated with decision-making role preferences, we also found that the effect of role preferences is still existent when controlling for age and education level. Previous studies indicated that demographics like age and education only explain 20% or less of the variability in preferences [29]. Additional explanation for differences in preferences could therefore be found in personality variables [30-32]. The role of personality traits in the involvement in the decision-making process should be investigated more thoroughly, so that interventions to support information provision and the decision-making process could be targeted more specifically.

The finding in this study that even four years after diagnosis a substantial part of the responders indicated a PDM role preference, although having gained knowledge about their condition and insights on the consequences of earlier decisions, is somewhat surprising. Other studies have found that if preferences are assessed retrospectively, more patients indicate a preference for a passive role, particularly in samples of cancer patients compared to non-cancer patients [33]. This could explain why still 20 percent of men indicated a passive role preference in this study. It could also be that experience with the decision-making process made patients more aware of the burden and difficulty of the decision they faced, increasing the tendency -in hindsight- to prefer a less active role. Increased stress levels and the feeling of being overwhelmed by the provided information are known to cause impaired cognitive processing [34, 35]. This could lead to preferring to simplify a complex situation by deferring the decision to a doctor overseeing all offered alternatives. Shared decision-making literature also suggests disentangling process involvement from the actual decision responsibility [36]. This implies patients still can have an active role in the process leading to the treatment decision, but prefer to leave to actual decision to the clinician.

We did not observe hospital specific effects on decision-making role preferences, which could indicate that the preferences indicated in this study represent a stable trait. Further, it may also indicate that there is a certain level of information provision all hospitals fulfill to but that the patients' role preference possibly does not fit this non-tailored approach in information provision.

The median time of 48 months between diagnosis and survey carries the risk for recall bias. However, if present, it is most likely that this bias is distributed randomly across all decision-making role preference groups in our sample. Although it is in the human nature that some information is forgotten over time, there is evidence that recall is not associated with age [37 38 39]. This could be an indication that our finding that older men prefer a passive role more than younger men is not caused by a group specific recall bias. Though, it should be taken in consideration that the receipt of information following Pca diagnosis is likely to be disturbed by the complex nature of the information and emotion involved to receiving the diagnosis [40]. Compared to that situation, our respondents were free from the distress of diagnosis and treatment decision-making at the moment of survey. This could reduce generalizability of our results to patients who are closer to diagnosis.

Another limitation of this study is that we only measured the preferred decision-making role post-treatment without having information about the actual role during treatment decision-making. While other studies report only small proportions of extreme discordance between preferred and experienced role, it is also known that role preferences can change during the decision-making process [5 7 36]. For this change in preference to occur, a patient must be aware of the importance of being involved. Often, patients assume there must be one superior treatment option instead of multiple preference-sensitive alternatives, and therefore not realizing the actual possibility to choose [1]. However, all patients in our sample have previous experience in treatment decision-making.

A major strength of this study was the population-based sample of Pca survivors that was available. Also, the response rate was high. However, the cross-sectional design of this study does not allow to determine causal relations between decision-making role preference and evaluation of information received. More research is needed to determine the direction in this relationship.

To broaden our understanding of the nature of role preferences and its relation with information provision and treatment decision-making, a prospective study should look into the process of patient involvement from the moment of Pca diagnosis. The role preferences identified in the current research could be interpreted as a trait, since evaluation took place long after diagnosis. This trait could lead to behavior or attitudes in patients that cause clinicians to provide less information or misinterpretation of preferred roles [41 42]. Distress following diagnosis or improved insight in the decision

could change the trait preference in a state preference for a more active or passive role DM [43, 44]. A longitudinal study is needed to look into the development of decision-making role preferences and its consequences for health outcomes [45].

CONCLUSION

We present evidence that the preference for a PDM role is associated with the perception of having received less information, less helpfulness of and satisfaction with the received information. This research suggests that current information provision practices do not optimally fit the needs of patients who prefer a PDM role compared to patients with a non-passive role preference.

CLINICAL IMPLICATIONS

Much of the information in clinical practice is given following standard formats. Clinicians should be aware of the fact that even if the provided information is objectively of good quality, it does not necessarily fit information needs of patients with a PDM role preference. For improving patient-centered care this further emphasizes the importance of assessing role preferences throughout the decision-making process and tailor both information provision and decisional support to these preferences.

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Chapter 3

THE IMPACT OF PROSTATE CANCER DIAGNOSIS AND TREATMENT DECISION-MAKING ON HEALTH-RELATED QUALITY OF LIFE BEFORE TREATMENT ONSET

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ABSTRACT

Objective – To test if patients' health-related quality of life (HRQoL) declines after prostate biopsy to detect Pca, and treatment decision-making in case Pca is confirmed, and whether personality state and traits are associated with these potential changes in HRQoL.

Methods – Patients who were scheduled for prostate biopsy to detect Pca (N=377) filled out a baseline questionnaire about HRQoL (EORTC QLQ-C30 and PR25), 'big five' personality traits (BFI-10), optimism (LOT-r), and self-efficacy (Decision Self-efficacy Scale) (t0). Patients with confirmed Pca (N=126), filled out a follow-up questionnaire on HRQoL within two weeks after treatment was chosen but had not yet started (t1).

Results – HRQoL declined between t0 and t1, reflected in impaired role and cognitive functioning, and elevated fatigue, constipation, and prostate specific symptoms. Sexual activity and functioning improved. Baseline HRQoL scores were unrelated to the selection of a particular treatment, but for patients who chose a curative treatment, post-decision HRQoL showed a greater decline compared to patients who chose active surveillance. Optimism was associated to HRQoL at baseline, decisional self-efficacy was positively associated to HRQoL at follow-up. No associations between HRQoL and the 'big five' personality traits were found.

Conclusion – Patients who have undergone prostate biopsy and treatment decision-making for Pca, experience a decline in HRQoL. Choosing treatment with a curative intent was associated with greater decline in HRQoL. Interventions aimed at optimism and decision self-efficacy could be helpful to reduce HRQoL impairment around the time of prostate biopsy and treatment decision-making.

1. BACKGROUND

An aging population and increased use of prostate cancer (Pca) screening contribute to a growth in Pca detection in The Netherlands and other Western countries [1-3]. When Pca is suspected, patients undergo prostate biopsy [4]. In The Netherlands only, at least 25,000 Dutch men undergo this procedure every year, resulting in approximately 10,000 Pca diagnoses (Netherlands Cancer Registry, 2015) [5]. The largest proportion of Pca diagnoses consist of localized cancer (stage I or II), for which surgery, radiotherapy (either brachy or external beam), and active surveillance (AS) are seen as equally acceptable treatments [4, 6]. However, adverse effects from treatment can impair patients' health-related quality of life (HRQoL) [7-10]. Common side-effects from treatments with curative intent (surgery, radiotherapy) include sexual, urinary and bowel-related complaints [9, 11], while AS can increase anxiety symptoms due to postponing treatment [12, 13]. Therefore, impact on HRQoL is an important factor when considering treatment options [14-16].

Changes in HRQoL after Pca treatment are well described, and generally consist of a major decline in HRQoL in the first 1-2 years after treatment [9, 17-19]. Besides the consequences of treatment, changes in HRQoL are related to psychological factors. Optimism and self-efficacy are associated with better HRQoL outcomes, while anxiety, depression and personality traits (e.g. neuroticism, distress) are associated with worse HRQoL outcomes [20-23]. However, most of these studies measured HRQoL from diagnosis onwards, lacking a pre-diagnosis baseline to also capture the psychological burden from prostate biopsy, receiving a Pca diagnosis, and treatment selection. Studies that did take a pre-diagnosis baseline, focused on a specific (older) patient population and did not measure immediately before and after diagnosis [24, 25].

To increase our understanding about the impact of Pca on HRQoL, including receiving a Pca diagnosis and choosing treatment, this study measured HRQoL pre-biopsy and post treatment decision-making. Our hypothesis was that a significant decline in HRQoL would already appear prior to treatment onset from the psychological burden of diagnosis and treatment decision-making. Moreover, we expected changes in HRQoL would be associated with psychological factors (personality traits, optimism, and self-efficacy).

2. METHODS

2.1 Participants and recruitment

Between January 2013 and May 2014, ten Dutch hospitals participated in this study and recruited 388 patients who were scheduled for a first prostate biopsy due to suspected Pca (M_{age}=66.5, SD=6.6; Figure 1). A host hoc power analysis revealed that this sample size was sufficient to achieve a power of .80 for detecting differences with an effect size from Cohen's *d*=.2 (with alpha .05). During consultation, patients were informed that the goal of the study was to investigate quality of care in prostate examination and quality of life of patients undergoing this procedure. Together with an information letter, patients received the first questionnaire (t0) on paper and a pre-stamped envelope to return the questionnaire. Follow-up questionnaires were sent to patients whose biopsy result confirmed Pca. These patients received this second questionnaire and a pre-stamped envelope at their home address within two weeks after treatment decision-making (t1). Diagnosis and the moment of treatment decision-making were monitored for all included patients from their (electronic) medical record. After review of the study protocol, the medical ethics review board of the initiating hospital waived the need for formal ethical approval (reference 2012.103) and all participating hospitals approved conducting the study. All patients signed informed consent.

2.2 Questionnaires

2.2.1 Demographics and clinical data

Participants were asked to indicate their age, education, marital status, last known prostate specific antigen (PSA) level, and choice of treatment. PSA levels were asked at both t0 and t1 to control for the possibility that treatment had already taken place before completing the t1 questionnaire.

2.2.2 Health-related quality of life

Health-related quality of life (HRQoL) was measured with the Dutch version of the EORTC QLQ-C30 questionnaire, which assesses functional HRQoL aspects (physical, role, cognitive, emotional, and social functioning, and global health) and symptoms common for cancer patients (fatigue, nausea, pain, dyspnea, sleep disturbance, appetite loss, constipation, diarrhea, and financial impact) [26]. The prostate cancer-specific EORTC QLQ-PR25 module was added to assess prostate cancer specific (urinary, bowel, and hormonal) symptoms and (sexual) functioning [27]. Scale reliability was low for the bowel and hormonal symptoms, and sexual activity subscale (alpha's 0.50-0.60), and adequate (alpha ≥0.70) for all other subscales. Similar scale reliability scores have been found earlier [27].

2.2.3 Psychological factors

As possible moderating variables, three measures for individual differences measures were included. First, the Big Five Inventory-10 (BFI-10) was included to measure *extraversion*, *agreeableness*, *conscientiousness*, *neuroticism*, and *openness;* also known as the 'big five' personality traits [28]. The BFI-10 was included in t0. With only two items per trait, low reliability scores were found (α<.50), which is common for this scale [29]. A subsequent confirmatory factor analysis confirmed five underlying factors, with each set of two items per trait yielding highest factor loadings.

Secondly, dispositional optimism, a generalized expectation that good things will happen, was assessed with the Life Orientation Test-Revised (LOT-R) [30]. Some minor textual adjustments were made to an existing and previously validated Dutch version of the LOT-R [31]. Scale reliability was sufficient (α=.67).

Thirdly, the Decision Self-Efficacy Scale was used as a subjective measure of the perceived ability to make a healthcare decision [32]. Rather than focusing on one specific decision, the goal of this scale was to measure feelings of self-confidence in a healthcare setting. The scale was included at t0 to measure a person's baseline decisional self-efficacy before the distress from diagnosis. In absence of an existing and validated Dutch version of this scale, a forward-backward translation was made by two researchers and the result was evaluated and consented on by two other researchers who were not involved to the translation. Scale reliability was good (α=.85).

2.3 Statistical analysis

Descriptive statistics are presented as means and standard deviations (SD) for continuous variables and as frequencies and percentages for categorical variables. Mean HRQoL scores at t0 were compared to the scores obtained at t1 using paired-samples t-tests. The association between personality traits and HRQoL scores were assessed using bivariate correlation analyses (Pearson's). Linear regression modelling was carried out with *global health* as dependent variable and personality characteristics as independent variables, controlling for age, education, PSA levels and diagnosis (dummy variable; for t0 only). All analyses were performed using SPSS version 22.0 (Statistical Package for Social Sciences, Chicago, IL, USA). *P*-values <.05 were considered statistically significant.

3. RESULTS

Three hundred and eighty eight patients gave informed consent of which 377 patients completed the first completed the first questionnaire (t0, response rate 97.2%). All patients whose biopsy confirmed Pca (n=126 patients, 32%), received the follow-up questionnaire (t1, response rate 63%) (Figure 1). There were no statistically significant differences in demographics between patients with cancer and patients without cancer at t0, between responders at t0 and t1, or between responders and non-responders at t1. Patient demographics are presented in Table 1.

3.1 Health-related quality of life

At the pre-biopsy baseline (t0), HRQoL did not differ between patients whose biopsy result confirmed Pca, and patients with a negative biopsy result (Table 2). After receiving diagnosis and treatment decision-making (t1), patients reported worse role and cognitive functioning and more symptoms (fatigue, constipation, urinary, bowel, and hormonal). Sexual activity and functioning improved after treatment was chosen (all with $p<0.05$, Table 2).

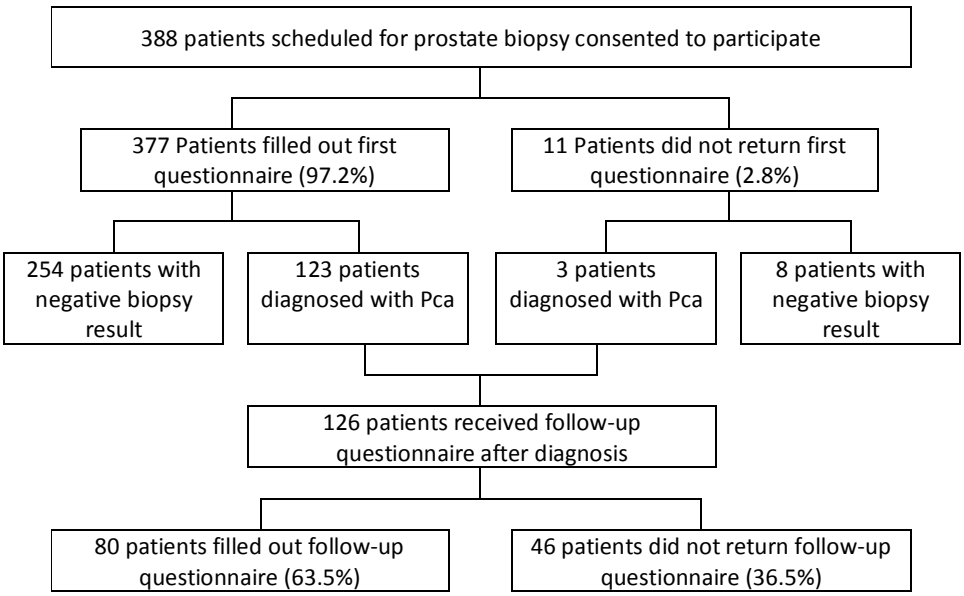

Figure 1. Patient flow

Table 1. Demographics

	t0 - No cancer (N=254)	t0 - Pca (N=123)	t1 - Pca (N=80)
Age at inclusion			
≤ 65 years	106 (44%)	40 (33%)	24 (30%)
66-75 years	115 (48%)	73 (60%)	50 (63%)
≥ 76 years	20 (8%)	9 (7%)	5 (6%)
Education			
Low	109 (43%)	48 (39%)	31 (39%)
Medium	60 (24%)	37 (30%)	25 (31%)
High	78 (31%)	36 (29%)	23 (29%)
Other/not specified	4 (2%)	2 (2%)	1 (1%)
Current occupation			
Employed	70 (28%)	28 (23%)	15 (19%)
Not employed	183 (72%)	93 (77%)	64 (81%)
Partnership			
Partner	224 (89%)	115 (94%)	74 (95%)
No partner	28 (11%)	7 (6%)	5 (6%)
Children			
Yes	228 (91%)	118 (96%)	77 (96%)
No	24 (9%)	5 (4%)	3 (4%)
Prostate Specific Antigen (PSA)			
≤ 5 ng/ml	42 (17%)	19 (16%)	19 (25%)
5.01-10 ng/ml	125 (49%)	59 (48%)	37 (49%)
≥ 10.01 ng/ml	85 (34%)	44 (36%)	20 (26%)
Selected treatment			
Active surveillance			26 (34%)
Radical prostatectomy			22 (29%)
Radiotherapy			28 (37%)

Numbers do not always add up to the same total due to item non-response
Differences between groups did not reach statistical significance

Table 2. HRQoL scores

	No Pca	Pca			
HRQoL core	**t0 (N=254) Mean (SD)**	**t0 (N=123) Mean (SD)**	**t1 (N=80) Mean (SD)**	**Mean difference (t1-t0)1**	
Global Health	83.5 (14.8)	83.7 (15.4)	80.7 (16.1)	-3.0	
Physical functioning	94.2 (10.4)	94.3 (10.1)	92.8 (12.7)	-1.5	
Role functioning	94.7 (14.9)	96.0 (12.9)	86.1 (24.2)	-9.9	***
Emotional functioning	85.3 (16.0)	85.0 (16.8)	83.4 (19.9)	-1.6	
Cognitive functioning	91.2 (15.0)	92.3 (12.5)	88.9 (16.9)	-3.4	*
Social functioning	95.0 (13.9)	96.2 (10.1)	93.9 (14.3)	-2.3	
Fatigue	11.4 (17.3)	10.7 (15.5)	17.0 (22.3)	6.3	**
Nausea/vomiting	1.0 (4.7)	1.1 (5.2)	2.4 (11.9)	1.3	
Pain	6.8 (15.8)	5.8 (12.6)	9.4 (19.8)	3.6	
Dyspnoea	7.7 (16.9)	6.5 (15.3)	6.8 (17.3)	0.3	
Insomnia	14.4 (23.8)	13.8 (21.5)	15.0 (25.6)	1.2	
Appetite loss	1.9 (8.2)	2.0 (7.9)	4.7 (16.8)	2.7	
Constipation	1.7 (8.0)	4.2 (12.7)	7.7 (20.0)	3.5	*
Diarrhea	4.0 (13.4)	3.4 (11.0)	6.8 (18.9)	3.4	
Financial difficulties	2.6 (12.3)	0.8 (5.3)	2.6 (12.9)	1.8	
Prostate specific					
Urinary symptoms	15.9 (13.4)	13.3 (11.8)	17.6 (15.6)	4.3	*
Bowel symptoms	3.0 (6.3)	2.7 (5.8)	5.6 (10.5)	2.9	**
Hormonal symptoms	3.5 (5.8)	3.8 (5.8)	7.0 (9.4)	3.2	***
Sexual activity	63.1 (21.6)	61.5 (22.2)	65.4 (21.3)	3.9	**
Sexual functioning	22.9 (20.3)	23.4 (19.6)	34.5 (24.0)	11.1	*

All scales are 0-100; for functioning subscales, full functioning is represented by a score of 100, for symptoms, absence of symptoms is represented by score of 0.
All comparisons at t0 between patients with and without cancer were non-significant
[1] Paired comparison t1 vs t0 (N=70)
* $p<.05$
** $p<.01$
*** $p<.001$

3.2 Treatment choice

In case Pca was detected, symptoms and functioning reported prior to biopsy (t0) was not associated to selection of a particular treatment. At the time point after treatment decision-making (t1), men who chose a curative treatment reported reduced functioning and more symptoms compared to men who selected AS (Table 3). No associations were found between treatment choice and personality characteristics (data not shown).

Table 3. HRQoL changes grouped per treatment decision

	AS N=23		Curative treatment (RP or RT) N=38		
HRQoL core	**t0 Mean (SD)**	**t1 Mean (SD)**	**t0 Mean (SD)**	**t1 Mean (SD)**	
Global Health	86.4 (15.8)	87.9 (10.5)	81.4 (14.4)	75.0 (18.8)	
Physical functioning	93.9 (10.1)	94.2 (10.7)	93.3 (13.2)	92.3 (15.3)	
Role functioning	97.0 (9.8)	97.0 (9.8)	95.5 (16.0)	79.7 (29.3)	**
Emotional functioning	89.8 (14.5)	92.0 (13.0)	85.1 (17.7)	77.6 (23.7)	*
Cognitive functioning	90.5 (13.5)	92.1 (10.2)	91.2 (12.1)	85.5 (20.9)	*
Social functioning	93.1 (11.0)	99.2 (3.6) *	96.8 (8.6)	90.5 (18.7)	*
Fatigue	10.1 (12.8)	8.6 (12.8)	10.5 (16.1)	21.6 (26.8)	**
Nausea/vomiting	3.0 (8.4)	2.3 (5.9)	0 (0.0)	16.5 (2.7)	
Pain	5.3 (14.9)	3.0 (8.4)	7.0 (14.3)	15.4 (25.8)	
Dyspnoea	7.6 (14.9)	6.1 (16.7)	7.9 (19.7)	8.8 (20.0)	
Insomnia	9.1 (15.2)	6.1 (16.7)	16.7 (24.2)	22.8 (31.1)	
Appetite loss	4.5 (11.7)	1.5 (7.1)	2.6 (9.1)	8.8 (22.8)	
Constipation	1.5 (7.1)	1.5 (7.1)	4.4 (13.8)	13.2 (26.3)	*
Diarrhea	3.0 (9.8)	3.0 (9.8)	4.4 (11.4)	11.4 (24.8)	
Financial difficulties	0.0 (0.0)	1.5 (7.1)	0.9 (5.4)	3.5 (17.0)	
Prostate specific					
Urinary symptoms	19.3 (12.9)	14.1 (10.4)	10.3 (8.7)	19.0 (18.4)	**
Bowel symptoms	2.2 (6.3)	2.2 (4.5)	3.1 (5.2)	8.6 (13.4)	*
Hormonal symptoms	3.9 (4.9)	5.6 (6.7)	3.0 (4.9)	6.4 (10.0)	*
Sexual activity	60.9 (27.3)	63.0 (18.1)	58.6 (20.3)	68.0 (20.9)	*
Sexual functioning	25.0 (17.9)	23.8 (19.6)	22.2 (16.4)	29.6 (18.4)	

All scales are 0-100; for functioning subscales, full functioning is represented by a score of 100, for symptoms, absence of symptoms is represented by score of 0.
AS = Active surveillance; RP = Radical prostatectomy; RT = Radiotherapy
* $p<.05$
** $p<.01$

3.3 Psychological variables

Prior to biopsy (t0), *optimism* was a significant predictor for *global health* (B=.31, $p<.001$). After receiving diagnosis and treatment decision-making (t1), a positive association was found between *global health* and *decisional self-efficacy* (B=.29, $p=.04$). Of the Big five traits, *extraversion* (B=.14, $p=.03$), and *neuroticism* (B=-.17, $p=.01$), were significant predictors for *global health* at t0, no relations were found at t1.

4. DISCUSSION

This study investigated the HRQoL impacts of undergoing prostate biopsy, receiving Pca diagnosis and choosing treatment. Prior to prostate biopsy, when Pca is suspected but not yet confirmed, HRQoL was similar between patients who were later confirmed to have Pca and patients without Pca. When a Pca diagnosis was received, and treatment was chosen but had not yet started, patients reported more symptoms and reduced functioning compared to the pre-biopsy baseline. HRQoL at baseline did not predict treatment choice, but patients who chose a curative treatment instead of AS, reported more symptoms and reduced functioning compared to patients who chose AS. Overall *global health* at baseline was related to *optimism*, after diagnosis and treatment selection an association with *decisional self-efficacy* was found.

4.1 HRQoL outcomes

Differences in HRQoL between patients who selected curative treatment over AS is not surprising. Men eligible for AS could be expected to be in a more favorable condition compared to men who need (immediate) curative treatment [33]. However, it is remarkable that most HRQoL differences were not present in our sample at baseline, but were only reported after diagnosis and treatment selection. Moreover, the highest level of urinary symptoms at t0 were reported by men who later selected AS, while after the treatment decision was made, most symptoms were reported by men who selected a curative treatment. Therefore, changes in HRQoL appear to be influenced by the impact of diagnosis and treatment decision-making, rather than by changes in the patient's physical condition. Possibly, the Pca diagnosis made men more aware of their symptoms and led them to attribute their overall condition more to their disease. Increased symptom burden and impaired functioning at t1 could also be explained by cognitive dissonance reduction [34]; consequently of a finalized treatment decision, men could be motivated to justify this decision as being the right one. This could have resulted in a revised HRQoL evaluation at t1 to make it consonant with the characteristics that would fit to the selected treatment [35, 36]. If biopsy itself caused a decline in HRQoL, all patients should have reported lower HRQoL at t1, while this was only the case for patients who chose a curative treatment, patients from the AS group even reported (non-significant) improvements [37].

Earlier studies on physical and psychological outcomes in Pca patients highlighted the perceived masculinity threat men could experience [38, 39]. This threat affects how men cope with their condition and the perceived threat could cause a further decline of HRQoL after treatment. Although most of the work on masculinity threats in Pca patients focused on post-treatment outcomes, it is likely that this perceived threat is already

present from diagnosis onwards. In our results, reduced role functioning and increased sexual functioning (compensatory behavior) could be indicative for the presence of a masculinity threat [40, 41].

4.2 Personality factors

Optimism and decisional self-efficacy were associated with better global health, this is in line with previous research that found optimism and decisional self-efficacy to be associated with less distress and better coping [21, 42]. In the current study, patients scoring higher on optimism report better HRQoL prior to biopsy, when Pca was suspected but not yet confirmed.. After diagnosis, and a treatment decision was required, optimism seemed to play less of a role and decisional self-efficacy, the subjective feeling of being able to take the right action, making good decisions and to ask questions, was positively associated to HRQoL. This adds to previous findings about knowledgeable (and therefore possibly more self-efficated) patients reporting better HRQoL [43].

Instead of focusing on a single trait (e.g. neuroticism), this study investigated a broader spectrum of the big five personality traits. At t0, extraversion and neuroticism were related to global health, while at t1 no relations were present anymore. Hence, we found no evidence of a moderating role of specific traits affecting changes in HRQoL. Another explanation could be that the brief measure we used was not sensitive enough to also detect statistically significant differences in the smaller t1 sample. Future studies should use more extensive measures to investigate this relation in more detail.

4.3 Study limitations

Some limitations need to be discussed. First, no detailed clinical data about tumor stage was available, and PSA was self-reported by participants. However, patients were only eligible for inclusion if Pca was suspected, following pre-biopsy screening (rectal examination and PSA testing). Therefore, we were still able to sample a homogeneous patient population. And although we had no registration of the number of patients refusing participation, the average Pca detection rate in our sample was similar to what was expected based on literature [5]. Secondly, drop-out of men without Pca diagnosis and non-response at t1 led to a limited number of patients per treatment group available for further analyses. Moreover, the comparison between t1 and t0 on group level had sufficient power, however, the subgroup comparisons were lacking power. As we found no statistically significant differences in patient characteristics between responders and non-responders, we estimate the risk for selection bias was low. Our results should therefore be seen as exploratory findings on the development of HRQoL in Pca patients with a pre-diagnosis baseline. Follow-up studies preferably use larger samples.

4.5 Future studies

Based on the changes in HRQoL we found in this study, future studies should focus on determining the impact of the individual aspects of undergoing biopsy, receiving Pca diagnosis, and selecting treatment. Compared to the current design, this would require an additional measurement in between receiving diagnosis and making a treatment decision.

Furthermore, the current study did not follow-up on patients with a negative biopsy result. To have a complete comparison of HRQoL after prostate biopsy, post-biopsy HRQoL should also be compared between patients with a positive and patients with a negative biopsy result. Recently, a prospective study found similar HRQoL before and after diagnosis between Pca patients on AS and a non-cancer control group, indicating HRQoL of patients on AS is similar to that of patients without cancer [44]. However, it would be interesting to investigate if decisional self-efficacy is still associated to HRQoL outcomes when no treatment decision has to be made.

4.4 Clinical implications

This study emphasizes the impact of undergoing prostate biopsy, receiving a Pca diagnosis, and selecting treatment. Clinicians' should be aware that optimism and decisional self-efficacy are associated to HRQoL prior to treatment onset. To ensure that optimism does not backfire post-treatment, it is important to ensure accurate risk perceptions in patients about the chances of treatment success and the occurrence of treatment side-effects. Interventions to stimulate shared decision-making, like decision aids, could be helpful for achieving this, as well as to contribute to patients' decisional self-efficacy levels [45].

4.5 Conclusion

So far, most studies investigating HRQoL in Pca patients have focused on the impact of treatment, while neglecting the psychological burden caused by diagnosis and the treatment selection process. This study showed that prior to treatment onset, patients reported reduced functioning, more symptoms and lower overall *global health,* in particular if a curative treatment was selected. During clinical counseling, managing optimism when Pca is suspected (before and after biopsy) and (decisional) self-efficacy when Pca is confirmed, could help to reduce the pre-treatment impact on HRQoL.

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Chapter 4

A GLOBAL, INCREMENTAL DEVELOPMENT METHOD FOR A WEB-BASED PROSTATE CANCER TREATMENT DECISION AID AND USABILITY TESTING IN A DUTCH CLINICAL SETTING

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ABSTRACT

Many new decision aids (DAs) are developed while aspects of existing DAs could also be useful, leading to a sub-optimal use of resources. To support treatment decision-making in prostate cancer (Pca) patients, a pre-existing evidence-based Canadian DA was adjusted to Dutch clinical setting. After analyses of the original DA and routines in Dutch Pca care, adjustments to the DA structure and content were made. Subsequent usability testing (N=11) resulted in 212 comments. Care providers mainly provided feedback on medical content, patients commented most on usability and summary layout. All participants reported the DA was comprehensible and well-structured and would recommend DA use. After usability testing final adjustments to the DA were made. The presented methods could be useful for cultural adaptation of pre-existing tools into other languages and settings, ensuring optimal usage of previous scientific and practical efforts and allowing for a global, incremental DA development process.

BACKGROUND

Decision aids (DAs) are tools designed to support the process of shared decision making (SDM) between patients and their clinician [1,2]. DAs can have multiple formats (e.g. leaflets, website), but should at least create choice awareness, offer balanced information and stimulate patients to consider their preferences [3]. In general, DAs are associated with increased knowledge, more accurate risk perceptions and more conservative treatment preferences [4]. The International Patient Decision Aids Standards (IPDAS) provides DA developers consensus-based criteria to ensure DA quality [5]. To help DA developers, a checklist is available that includes nine categories to which the DA should comply (e.g. Provide sufficient information about the decision and using high quality evidence) [6].

A particularly fruitful area for the application of DAs is prostate cancer (Pca) care. Pca is the most common cancer in men in the Western world [7]. Pca treatment guidelines do not indicate a single superior treatment option but recommend a shared treatment decision between clinician and patient [8]. However, selecting the best suiting treatment from the available alternatives can be a burden for many patients. The process involves careful consideration of the risks and benefits of multiple treatments and weighing this against preferences and personal characteristics. Decision-making is further complicated by sub-optimal information provision and a possible misinterpretation of patient preferences by clinicians, which emphasizes the potential benefits from DAs in Pca care [9-11].

Recent reviews of Pca DA trials concluded that current Pca DAs provide good quality information and help to increase patients' knowledge [12,13]. Despite improved information provision, current DAs do not guarantee that SDM takes place. Moreover, content, format and presentation of Pca information within DAs varied substantially, with many failing to comply to all components of the IPDAS criteria [12,13]. The most identified shortcomings consisted of not including physicians and patients during DA development, a lack of balanced information on all options and the absence of explanation about the evidence used in the DA [13]. Rather than resolving these issues with current tools, often new tools are developed elsewhere. This further increases the variety and number of available tools, though routine use in clinical practice of these tools remains limited [14].

As many care providers articulated the need for a suitable Dutch DA, we built an interactive website based on an existing evidence-based online Canadian DA, developed by Feldman-Stewart and colleagues [15-19] as a starting point for further development in the Dutch situation. This paper describes the development process of the DA and usability evaluation in Dutch clinical setting.

METHODS

The DA development process and usability testing among relevant user groups consisted of six stages and was based on the model described by Kushniruk [20]. This model describes the typical system development starting from initial analysis, prototype development and evaluation, but allows for more input and changes in every development step compared to more traditional methodologies that have a fixed order of steps. Each stage was worked on by a multidisciplinary development team of urologists, psychologists and engineers (N=6). This section will discuss the stages in the development process, the final DA as outcome is described in the results section.

Stage 1: Translating the pre-existing DA

The background and validation of the existing Canadian DA has been described thoroughly, with particular focus on the information needs of Pca patients when making a treatment decision [15-19]. The validity of all topics covered by the original DA for Dutch patients was also confirmed by an earlier cross-country comparison (including The Netherlands) of information needs in prostate cancer patients [21]. Therefore, all content from the original DA was translated from English to Dutch.

Stage 2: Evaluating Dutch clinical routine

To investigate typical conversation flow in consultations about Pca treatment decision-making, all non-clinicians within the development team observed consultations between patients and urologist in the outpatient clinic of the initiating hospital. In addition to these observations of actual consultations, role playing was used to emphasize the steps clinicians usually take in treatment decision-making consultations with a patient. Role playing was performed by the two clinicians involved in the development team, with one of them simulating the patient role. Other members from the development team observed with special focus on the structure of the simulated consultations.

Stage 3: DA re-design

Following the observations from stage 2, the original DA was re-designed to fit with typical conversation flow as observed in stage 2. Moreover, the translated textual content from stage 1 was further adjusted to comply with Dutch and European treatment guidelines. All content was re-written according to standards for creating web-based text to ensure readability and comprehensibility for all literacy groups (e.g. maximum of 10-15 words per sentence and 5-10 sentences per paragraph, clear headings and

active phrasing) [22 23]**.** Readability and comprehensibility was later assessed by an expert in medical communication from the initiating hospital, who was not involved to the further development of the DA.

Stage 4: Development of explicit values clarification exercises

For use in patient decision aids, IPDAS defines that values clarification exercises (VCEs) should 'help patients to clarify and communicate the personal value of options', in order to ultimately increase congruence between personal preferences and the selected treatment option [24]. However, without clear design guidelines for VCEs a variety of exercises have been developed with little knowledge about which features actually work best [25-27 28] . A recent review suggests that VCEs should at least include trade-offs between option attributes in order to encourage value congruent decision-making [29]. Therefore, from all topics covered in the DA, those topics that differentiate between treatments were selected to create explicit VCEs. To present these topics as a trade-off, statements were presented in such way that an answer to each statement was related to a (type of) treatment. VCEs were developed within the development team and reviewed from the perspective of the disciplines present in the development team (urology, psychology, engineering design). After consensus by the development team, VCEs were added to the DA. The content and phrasing of the VCEs was further evaluated during usability testing.

Stage 5: Usability testing

After completion of the first version of the adjusted DA a usability test was conducted among patients and care providers (N=11).

Setting and participants

Participants for usability testing were recruited in the initiating hospital in the southern region of The Netherlands, by the clinicians from the development team. Four urologists (not involved to the DA development), two oncology nurses, one radiation oncologist and four Pca patients with recent experience in Pca treatment decision making agreed to participate in usability testing. All patients were between 55 and 65 years of age and within six months of Pca diagnosis. Patients with experience in the decision situation were selected because they were expected to be better able to imagine the situation of just having received a Pca diagnosis [30]. IPDAS therefore also requires that DA testing is performed by experienced patients [6]. Care providers were included in this usability test to ensure the DA content and usability would match their usual routines and their experiences with patients facing Pca treatment decisions. Also, care providers' review during development is required by IPDAS [6]. All care providers included in usability

testing were affiliated to the initiating hospital, but not involved in any other stage of DA development. Care providers ages ranged from 35 to 60 and all had a minimum of five years of experience in their current position. All participants were instructed to use the DA from the perspective of a patient diagnosed with low-risk Pca and eligible for all four treatments covered in the DA (active surveillance, surgery, brachytherapy, external beam radiotherapy). No specific further usage instructions were given in order to let participants use the DA as naturalistically as possible.

Participants were asked to think aloud when navigating through the DA and to mention every remark or difficulty they encountered during DA usage. This procedure is commonly used to investigate human-computer interactions and has been applied before for DA usability testing as well [31]. The usability test was run in two simultaneous sessions in the outpatient clinic of the initiating hospital, with two observers from the development team present in each session. The observers monitored if the participants' verbalization matched their DA usage (e.g. saying navigation was easy accompanied by clicking on the correct buttons). As the DA only consists of a limited number of steps, if any action was not verbalized by the participant, a clarifying question was asked to the participant. During DA usage participants did not receive further feedback or other instructions from the observers. Each participant was given 30 minutes to use the DA followed by a fifteen minute semi-structured interview. The goal of the interview was to reflect on DA usage in addition to the comments made while using the DA. Interviews are commonly added to think-aloud procedures to ensure that the most important aspects have been covered during the usability test and to reduce the risk of bias in the interpretation of participants' verbalizations [32]. The interview covered five questions asked to all participants: 1. 'What were your expectations upfront?' 2. 'What is your first impression of the DA?' 3. 'Was the information understandable and useful?' 4. 'What were positive aspects?' 5. 'What can be improved?' Only patients were then asked: 1. 'Would you recommend this to other patients?' and 2. 'What feeling did the DA gave you?' Care providers were asked if they would offer this DA to patients. Participants were then thanked for their participation and received a bottle of wine as token of appreciation for participating.

Measures and Analysis

As a first step, all notes from all sessions and observers were combined and labeled as either general comments about the DA or related to a specific section of the DA. All comments were then further categorized to Usability, Layout, Language, Content, Amount, Values Clarification or DA Summary. Next, the accuracy and urgency of all

comments was discussed by the development team to determine the implications for DA adjustments. If consensus was reached on the need for changes, this led to final adjustments in the DA.

Stage 6: Final adjustments

Usability testing resulted in final adjustments to the DA (described in Results section). Finally, the DA was evaluated for compliance with the IPDAS criteria [6].

RESULTS

Decision aid

Stage 1 resulted in a plain text translation of the original Canadian DA on a prototype website. From the observations of conversation flow in clinical practice (stage 2) it was learned that following diagnosis clinicians often do not go into detail about all treatment options immediately. If eligible for active surveillance, treatment options are first presented as a consideration between active surveillance and curative treatment, before curative treatments options are discussed in more detail. In order to tailor the DA to this typical conversation flow during consultation, the DA was designed into four steps. Table 1 provides an overview of all topics covered in DA steps 1 to 3.

DA step 1: General Pca information

This introducing step provides background information about Pca in general. The anatomy of the prostate and the commonly used terms PSA and Gleason are explained.

DA step 2: Active surveillance versus curative treatment

The pros and cons of not treating immediately are compared to (immediate) curative treatment (Table 1). Specific treatment characteristics are not yet discussed in detail. Step 2 ends with VCEs on topics that require trade-offs between curative treatment and AS (Table 2).

DA step 3: Surgery versus radiotherapy

If patients are still undecided or have a preference for curative treatment following step 2 they continue to step 3. This step explains the difference between surgery and radiotherapy in more details (Table 1). An example page from this step is provided in figure 1. Patients who already prefer AS after step 2 are allowed to skip this step. Step 3 ends with VCEs on topics that differentiate between surgery and radiotherapy (Table 2). If patients already indicated a preference for AS in step 2, continuing with step 3 is optional.

Table 1. Content covered in Dutch DA

Step 1: Introduction
What is prostate cancer?
What do PSA and Gleason mean?
How does prostate cancer progresses?
What is the effect on my life expectancy?
Step 2: Curative treatment versus active surveillance
What is active surveillance?
What treatments are there?
What are the advantages?
What are the disadvantages?
What are the risks?
What is the chance of a rising PSA?
What is the risk of dying from prostate cancer?
Step 3: Surgery versus radiotherapy
What is the procedure for surgery?
What is the procedure for radiation therapy?
What are the advantages?
What are the disadvantages?
What is the risk for erectile dysfunction?
What is the risk for bladder dysfunction?
What is the risk for bowel problems?
How do I know if treatment was successful?
What if the cancer progresses or treatment is not successful?

DA step 4: Summary

An overview of how many topics have been read and the responses to VCEs are provided in a printable summary at the end of the DA (figure 2). This summary can be taken by the patient to the next consultation with the clinician in order to further facilitate shared decision-making. Alternatively, the summery can be accessed online during consultation.

Table 2. DA Values clarification Exercises (VCEs)

Step 2: Curative treatment versus active surveillance		
Topic	**Reasons for active surveillance**	**Reasons for treatment**
Acceptance of deferring treatment	I am confident enough that I will be treated on time	I do not want to postpone treatment because I do not want to be too late
Avoiding possible unnecessary treatment	If treatment might be unnecessary,I would rather wait	I prefer treatment,even if it might be unnecessary
Acceptance of treatment side-effects	I find possible treatment side effectslike erectile and urinary dysfunctions difficult to accept'	I find the possible treatment side effects acceptable'
Step 3: Surgery versus radiotherapy		
Topic	**Reasons for surgery**	**Reasons for radiotherapy**
Treatment procedure	I find it important that all cancer cells are removed from my body	I find it important that the cancer cells die andnot grow further
Treatment side-effects	I find bowel problems worse than incontinence	I find incontinenceworse than bowel problems
Secondary treatment	I am comforted by the thought that I can have radiation if surgery is unsuccessful	I accept that surgery is difficultafter radiation
Fear for surgery	I am not anxious about surgery	I am anxious about surgery

Usability testing

Usability testing resulted in 212 usability and content comments. Care providers mainly reported feedback on the specific radiotherapy related content, a need for more descriptive notes to accompany the illustrations and risk representations. Patients mainly reported usability remarks and comments about the DA summary section. All participants reported that the writing style was comprehensible and that the DA structure and navigation were clear. A summary of the results from the think-aloud procedure and interview results are presented in Table 3. In addition to the usability items, all care providers (100%) indicated they would offer the DA to patients and all patients (100%) indicated they would recommend the DA to other patients. After discussion of the results in the development team, three main adjustments to the final DA were made: (1) accompanying legends were added, (2) radiotherapy content was adjusted, and (3) the DA summary section was simplified. The final version of the DA complied to all IPDAS criteria [6] (Table 4).

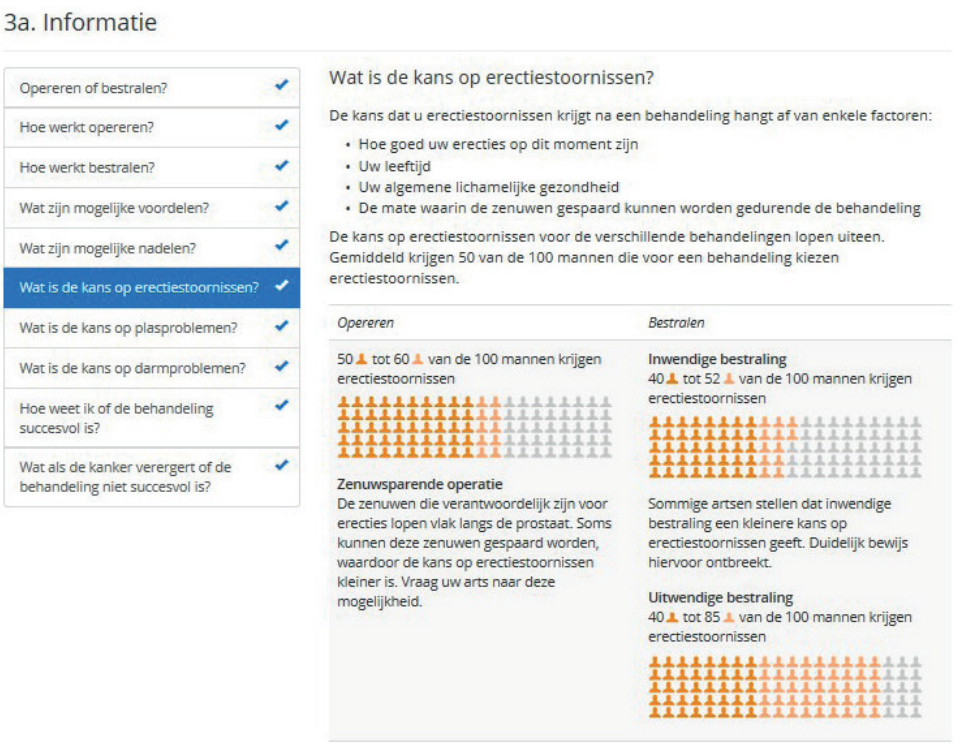

Figure 1. Screen from DA step 3, information about active treatments

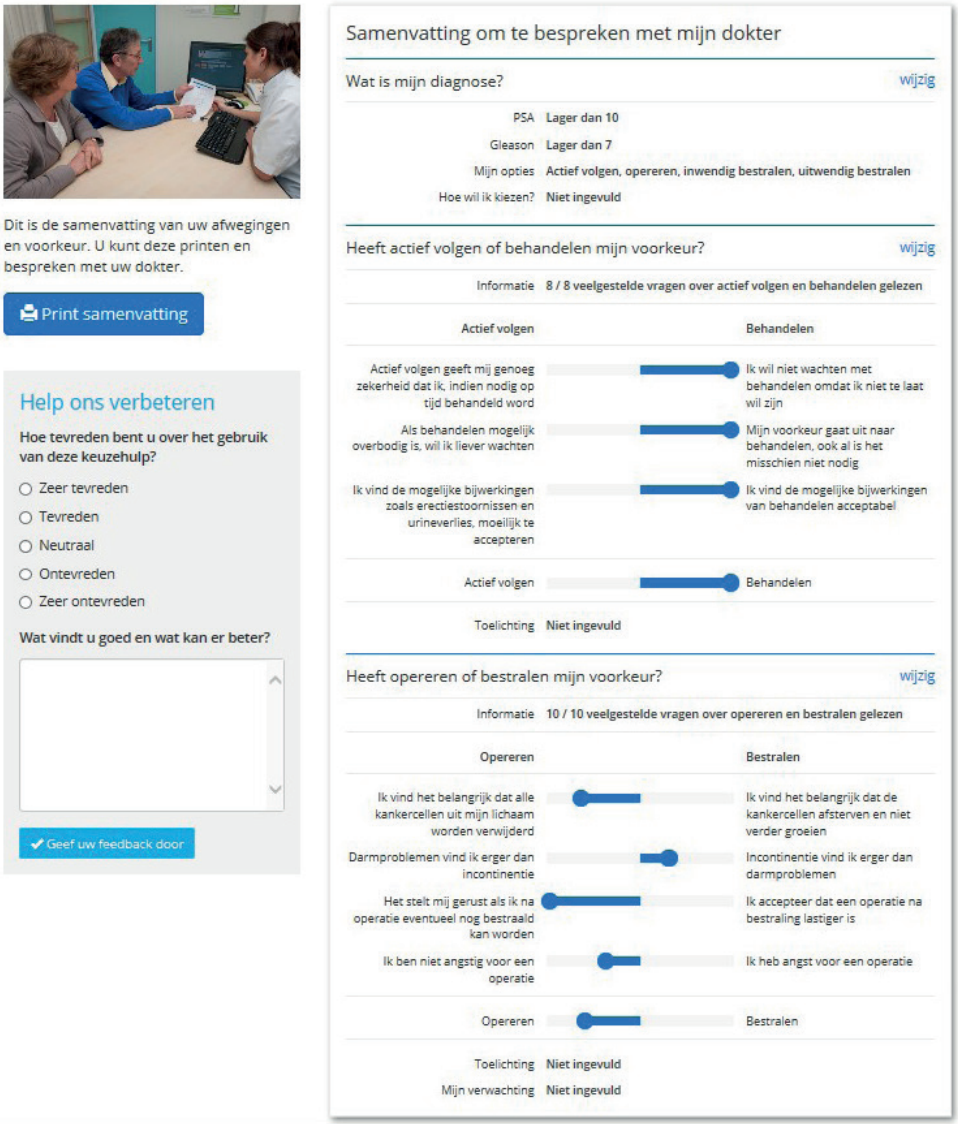

Figure 2: DA summary page

Table 3. DA usability test summary

Category	Number of comments	Key findings	Representative quotes	Implications
Usability	41	Usage of the DA was intuitive and easy	Hardly needed any instructions Navigated smoothly, without extra instructions User-friendly	No need for changes to improve usability
Layout	26	The layout was clear and supportive of making comparisons and trade-offs	Layout is clear Structured The differences are presented next to each other, that helps in the trade-off	No need to change the DA layout
Language	17	Used language is suitable for target group	Clear language Comprehensive language	No need to change the writing style
Content	35	Content is complete and balanced	All pros and cons per option are named clearly Good explanations	The general content was approved, but some aspects need adjustments;
	12	Some risk information is difficult to understand	Are these numbers correct? What does this figure mean? What does the difference in color mean in the figures?	Descriptive notes and legends should be added to illustrations and risk figures
	30	Some details of the radiotherapy procedure needs adjustment or further elaboration	Brachytherapy also involves a surgical aspect External beam radiotherapy affects the entire prostate, not solely the tumor	Radiation therapy content should be refined
Amount	16	Presented information is complete but can be redundant if all sections are read	Very complete Still very information dense Repetition in some texts	Patients should be allowed to skip parts that are not relevant to them, the message indicating this should be more prominent. The amount of information is needed to enable an informed decision.
Values clarification	15	Exercises are understood and used correctly	Statements help to weigh options	
Summary	20	The summary is not clearly recognized as a summary and natural ending of the DA	Is this the end of the DA? What does it mean that I have read 4 out of 4 themes? Some representation of personal situation would be nice	Summary was not recognized as being the end of the DA. Headings should more clearly indicate that a summary is presented. The clinical information entered at DA start (PSA, Gleason, eligible treatments) should also be displayed in the summary
Total	**212**			

Table 4. IPDASi v3 Checklist

Dimension	Item	Result
Information	1. The decision support technology describes the health condition or problem (intervention, procedure or investigation) for which the index decision is required	✓
	2. The decision support technology describes the decision that needs to be considered (the index decision)	✓
	3. The decision support technology describes the options available for the index decision	✓
	4. The decision support technology describes the natural course of the health condition or problem, if no action is taken.	✓
	5. The decision support technology describes the positive features (benefits or advantages) of each option	✓
	6. The decision aid describes negative features (harms, side effects or disadvantages) of each option.	✓
	7. The decision support technology makes it possible to compare the positive and negative features of the available options.	✓
	8. The decision support technology shows the negative and positive features of options with equal detail (for example using similar fonts, order, and display of statistical information).	✓
Probabilities	1. The decision support technology provides information about outcome probabilities associated with the options (i.e. the likely consequences of decisions)	✓
	2. The decision support technology specifies the defined group (reference class) of patients for which the outcome probabilities apply.	✓
	3. The decision support technology specifies the event rates for the outcome probabilities (in natural frequencies).	✓
	4. The decision support technology specifies the time period over which the outcome probabilities apply.	✓
	5. The decision support technology allows the user to compare outcome probabilities across options using the same denominator and time period.	✓
	6. The decision support technology provides information about the levels of uncertainty around event or outcome probabilities (e.g. by giving a range or by using phrases such as "our best estimate is…")	✓
	7. The decision support technology provides more than one way of viewing the probabilities (e.g. words, numbers, and diagrams).	✓
	8. The decision support technology provides balanced information about event or outcome probabilities to limit framing biases.	✓
Values	1. The decision support technology describes the features of options to help patients imagine what it is like to experience the physical effects.	✓
	2. The decision support technology describes the features of options to help patients imagine what it is like to experience the psychological effects.	✓
	3. The decision support technology describes the features of options to help patients imagine what it is like to experience the social effects.	✓
	4. The decision support technology asks patients to think about which positive and negative features of the options matter most to them.	✓

Table 4. Continued

Dimension	Item	Result
Decision Guidance	1. The decision support technology provides a step-by-step way to make a decision.	✓
	2. The decision support technology includes tools like worksheets or lists of questions to use when discussing options with a practitioner.	✓
Development	1. The development process included finding out what clients or patients need to prepare them to discuss a specific decision	✓
	2. The development process included finding out what health professionals need to prepare them to discuss a specific decision with patients	✓
	3. The development process included expert review by clients/patients not involved in producing the decision support technology	✓
	4. The development process included expert review by health professionals not involved in producing the decision aid.	✓
	5. The decision support technology was field tested with patients who were facing the decision.	✓
	6. The decision support technology was field tested with practitioners who counsel patients who face the decision.	✓
Evidence	1. The decision support technology (or associated documentation) provides citations to the studies selected.	✓
	2. The decision support technology (or associated documentation) describes how research evidence was selected or synthesized.	✓
	3. The decision support technology (or associated documentation) provides a production or publication date.	✓
	4. The decision support technology (or associated documentation) provides information about the proposed update policy.	✓
	5. The decision support technology (or associated documentation) describes the quality of the research evidence used.	✓
Disclosure and transparency	1. The decision support technology (or associated technical documentation) provides information about the funding used for development.	✓
	2. The decision support technology includes author/developer credentials or qualifications.	✓
Plain Language	1. The decision support technology (or associated documentation) reports readability levels (using one or more of the available scales).	✓
DST Evaluation	1. There is evidence that the decision support technology improves the match between the features that matter most to the informed patient and the option that is chosen	✓
	2. There is evidence that the patient decision support technology helps patients improve their knowledge about options' features	✓

DISCUSSION

This paper describes the development of a Dutch Pca treatment DA, based on an evidence-based Canadian Pca treatment DA and the subsequent usability testing among relevant user groups. Results of usability testing show that the DA was evaluated positively by patients and care providers and both groups would recommend use of the DA in clinical practice. The described development method could be useful for adaptation of other pre-existing and validated tools to different cultural or local circumstances.

Development of DAs is an effortful process and usually involves multiple rounds of assessing needs, required content and preferred structure among patients and care providers [33]. An important benefit of the proposed model of adapting a pre-existing tool is that these steps are already taken. For the current DA, the content was previously validated [15-19], and a cross-cultural comparison also confirmed importance of the included topics to Dutch patients [21].

The availability of validated content made it possible to focus more on the fit between DA structure and typical conversation flow in routine clinical practice. Many DAs have been developed for use independent from the consultation [34], which may have led to a suboptimal fit between conversation flow during consultation and DA structure. A known barrier related to limited DA uptake in clinical practice is that clinicians often find DAs impractical to use or that other consultation specific factors limit structural DA implementation [35]. Therefore, additional observations of clinical consultations and role playing took place and identified a two-step approach in discussing Pca treatment alternatives with patients. Instead of offering four alternative treatments simultaneous, a first step contains choosing between active surveillance and curative treatment and a second step discusses curative treatments in more detail. By also transferring this two-step approach from consultation into the DA, it is expected that patients experience a more natural fit between consultation and DA usage. Moreover, the DA provides direct support to the clinician's explanation.

To further improve facilitation of SDM we added two features to the DA. First, VCEs were developed and added to the DA. Second, the DA ends with a printable summary of preferences and responses to the VCEs that the patient can bring to his clinician for discussion. The summary provides the clinician with insight on what matters most to the patient and to what extent the patient has formed a preference or is still undecided. The following consultation and additional decisional support (e.g. consultations with

nurses, radiotherapists) can then be adjusted accordingly. A cluster RCT is in progress to evaluate the efficacy of this DA and to test whether decision outcomes align with patients' preferences and values [36].

Literature reports mixed findings from using VCEs in DAs and provide no clear guidelines for VCE design [25, 26, 28, 37, 38]. However, there are indications to assume the benefit of VCEs emerge after the decision is made and that VCE design should at least incorporate trade-offs between treatment attributes [19, 29]. In the absence of design guidelines, further development of the VCE within the current DA was based on consensus within the development team. However, future research should look into the effectiveness of the VCE features used in this DA.

A specific aspect that needs to be investigated further is the labeling of VCE outcomes. For the current DA, the development team decided to label VCEs outcomes with corresponding treatments. With a strong initial treatment preference (pre-DA) it could be that labeling may lead to patients seeking confirmation of their initial preference rather than achieving actual preference elicitation or misinterpreting information [39]. However, for clarity reasons we believed the VCEs should have labeled outcomes to make patients aware of the consequence of their preference (e.g. when valuing incontinence worse than bowel problems, a patient should place radiation therapy over surgery on this topic). With this insight the responses to the VCE contribute to the construction of an informed treatment preference. We expect labeled VCEs support this process better compared to unlabeled items. To gain more understanding on the development and usage of VCEs, more studies are needed to investigate VCE effectiveness and optimal presentation formats.

A potential limitation of the current development and usability test was the relatively small sample used in usability testing (N=11). However, our sample included all relevant user groups; patients, urologists, nurses and a radiotherapist. All participants in usability testing consented on the usability and acceptability of the DA to a point where it seemed saturation was reached and it was not expected additional participants would have resulted in new insights. The point of saturation in qualitative research is often reached within 6 to 12 participants [40].

CONCLUSION

The newly developed Dutch Pca treatment DA was evaluated positively by patients and care providers, both groups would recommend DA usage to others. Patients consented on easy usability and care providers confirmed the accuracy of the provided information.

Adapting an existing tool to a (culturally) different setting and adjusting it to local circumstances seems a useful alternative to an entirely new development process. This could free resources to focus on other important aspects like DA implementation.

Practice implications

The process of developing and testing the DA as described in this paper could be applied to the (cultural) adaptation of other pre-existing tools to different languages and clinical settings. As it enhances focus on usability and fit with clinical practice, it could be a fruitful step to improve implementation of decision aids in routine clinical care.

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Chapter 5

IMPACT OF A WEB-BASED TREATMENT DECISION AID FOR EARLY-STAGE PROSTATE CANCER ON SHARED DECISION-MAKING AND HEALTH OUTCOMES: STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL

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Trials 2015; 16:231

ABSTRACT

Background: At an early stage, prostate cancer patients are often eligible for more than one treatment option, or may choose to defer curative treatment. Without a pre-existing superior option, a patient has to weigh his personal preferences against the risk and benefits of each alternative to select the most appropriate treatment. Given this context, in prostate cancer treatment decision-making, it is particularly suitable to follow the principles of shared decision-making (SDM), especially with the support of specific instruments like decision aids (DAs). Although several alternatives are available, present tools are not sufficiently compatible with routine clinical practice. To overcome existing barriers and to stimulate structural implementation of DAs and SDM in clinical practice a web-based prostate cancer treatment DA was developed to fit clinical workflow. Following the structure of an existing DA, Dutch content was developed and values clarification methods (VCMs) were added. The aim of this study is to investigate the effect of this DA on (shared) treatment choice and patient reported outcomes.

Methods/design: Nineteen Dutch hospitals are included in a pragmatic, cluster randomized controlled trial, with an intervention and a control arm. In the intervention group, the DA will be offered after diagnosis, and a summary of the patients' preferences, which were identified with the DA, can be discussed by the patient and his clinician during later consultation. Patients in the control group will receive information and decisional support as usual. Results from both groups on decisional conflict, treatment choice and the experience with involvement in the decision-making process are compared. Patients are requested to fill in questionnaires after treatment decision-making but before treatment is started, and 6 and 12 months later. This will allow the development of treatment satisfaction, decisional regret and quality of life to be monitored. Clinicians from both groups will evaluate their practice of information provision and decisional support.

Discussion: This study will describe a web-based prostate cancer treatment DA with VCMs. The effect of this DA on the decision-making process and subsequent patient reported outcomes will be evaluated.

Trial registration: The Netherlands National Trial Register NTR4554**,** registration date 1 May, 2014.

BACKGROUND

Prostate cancer (Pca) is the most common malignancy in men in the western world, and in The Netherlands where more than 10,000 new prostate cancer patients are diagnosed each year [1]. Incidence is still growing due to earlier detection and an ageing population [2-4]. Based on demographic developments only, the incidence of prostate cancer in The Netherlands is expected to increase by 49% between 2011 and 2030 [5].

For the treatment of localized (low and intermediate risk) prostate cancer, the most common curative treatment options include radical prostatectomy, external beam radiotherapy (EBRT), and brachytherapy. Each curative treatment option has a specific risk profile concerning the occurrence of treatment side effects (for example. impotence, incontinence, and bowel problems). Because curative treatment may not always be necessary as initial treatment for low-risk Pca, active surveillance can be considered a valid option for avoiding or deferring the need for curative treatment. Active surveillance has some known psychosocial barriers like anxiety and uncertainty about disease progression which can withhold patients from choosing this option, although active surveillance is increasingly applied in clinical practice [6,7]. Clinical practice guidelines do not provide strong treatment recommendations given a lack of convincing evidence indicating superiority of any of the available options [8]. Choosing the most suitable treatment option therefore requires a patient to evaluate the treatment procedure, risk for side-effects and the chance of success for all available options. Combined with personal preferences and characteristics, identifying the best suitable treatment option is a difficult and stressful exercise for many patients [9,10]. Further complicating factors are clinicians' misinterpretation of patients' preferences, (information) needs and the patient's preferred role in the decision-making process [11-15]. Eventually, this may result in the clinician dominating in the treatment decision-making at the expense of the patients' preferences. It is possible that expressing a dominant clinician view may contribute to observed regional variations in the management of prostate cancer [16-20].

During the past decade, several decision aids (DAs) have been developed with special focus on prostate cancer care. Instruments range from information booklets to tailored web-based tools. The variety in the formats used may have contributed to the finding that effects on decisional outcomes have been inconsistent across randomized trials and that no effects on choice have been found [21,22]. Systematic reviews further emphasize that many previous studies are at high risk of selection bias due to inadequate concealment or blinding of data collectors and outcomes assessors, and that more studies are needed to determine how DAs can be implemented best in clinical practice [21,22].

Determining the effect of a DA intervention and finding optimal implementation methods are both aims of the current trial. A web-based prostate cancer treatment DA was developed to fit with Dutch clinical workflow. Based on the structure of an existing DA developed by Feldman-Stewart and colleagues [23,24], Dutch content was written and values clarification methods (VCMs) were added. Adaptation of the DA was based on the International Patient Decision Aid Standards (IPDAS) [25].

METHODS/DESIGN

Objectives and hypothesis

The main objective of this study is to investigate the impact of the DA on shared decision-making and treatment choice. It is hypothesized that DA usage will improve prostate cancer knowledge and satisfaction with information provision and therefore better prepare patients for clinical encounters and the following decision-making, which will result in lower levels of decisional conflict compared to standard care. Further, it is expected that better knowledge and less decisional conflict will also result in improved treatment satisfaction, less regret and ultimately improved health-related quality of life (HRQoL). In terms of actual choice we expect less variation in selected treatments in the intervention group compared to the control group.

A secondary aim is to investigate optimal implementation, as previous studies have emphasized the need to gain more insight on this matter [21]. From the patient perspective it is expected that some subgroups will experience more benefit from DA usage than others. To identify these groups, the moderating role of age, preferred role in the decision-making process, specific health skills (for example, health numeracy and literacy) and personality on the main outcomes will be investigated. Healthcare providers in the intervention group will be asked their opinion about implementation of the DA. This will be compared with an evaluation of information provision and decisional support as provided by healthcare providers in the control group.

Study design

The design for this study is a two-armed pragmatic, cluster randomized controlled trial (CRCT). Clustering is performed at the hospital level, meaning that all included patients from a participating hospital are in the same study group. Participating hospitals can therefore provide the same type of care to all of their patients, making a CRCT less prone to contamination bias [26]. The study will be longitudinal, including patients immediately after prostate cancer diagnosis and following them for 12 months. Patient-reported

outcomes from both arms will be compared. Involved healthcare professionals will be included in a survey-study to evaluate their opinion on working with the DA. A comparison will be made with procedures of usual care from the control group.

The description of this design follows the CONSORT recommendation for reporting on trials (www.consort-statement.org) with the extensions for pragmatic [27] and cluster [28] randomized trials.

Randomization

Nineteen Dutch hospitals have been randomized to either 'usual care' (arm 1) or 'usual care + DA' (arm 2). With this so-called pre-randomization, the conventional sequence of obtaining informed consent followed by randomization is reversed [29]. This pre-randomization is needed because we make clinicians aware (when introducing the DA) of the principles of shared decision-making and the characteristics of the DA. This could affect the control group if they were recruited within the same hospital.

To prevent potential imbalance between the two arms that could arise from hospital characteristics (for example, hospital size and treatment profile), two strata were included in the randomization procedure. First, if cooperation between two hospital locations leads to overlap in medical staff or patients visiting both locations, there is a risk for contamination bias if these hospital locations are not in the same cluster. In our sample, four pairs of hospitals have this overlap in hospital staff or patient visits. To maintain variability in hospital characteristics within each cluster, only two pairs were allowed to enter the same cluster. The second criterion is related to hospital specific treatment variation. In The Netherlands, hospitals that perform robot-assisted radical prostatectomy indicate a significant larger proportion of their patients for surgery compared to other hospitals [4]. At the moment of randomization, three hospitals from our sample are known for having robotic surgery facilities to treat prostate cancer patients, and only two of these hospitals were allowed to join the same cluster.

Randomization was performed by a statistician not involved in the study and blind to the identity of the hospitals, using SPSS version 19.0 (Statistical Package for Social Sciences, Chicago, IL, USA). As a first step, the four paired hospitals were randomized (block size = 2). Next, the remaining 11 hospitals were also block randomized (block size = 6, with the last position unused). A set seed was chosen that fulfilled to the criteria that only two robot facilitated hospitals were allowed into the same cluster. The generated group order was then applied to a pre-existing list of participating hospitals, which was sorted in alphabetical order. As there is an uneven number of hospitals participating in this study, the largest cluster that was formed was identified as intervention cluster.

Study population, inclusion criteria and exclusion criteria

The DA is developed for the initial treatment decision in early-stage prostate cancer. In order to be eligible to participate in this study, a subject must meet the following inclusion criteria:

1. Patient is diagnosed with low or intermediate risk prostate cancer (EAU/ESTRO criteria) [30].
2. Patient is eligible for at least two of following treatment options: active surveillance, radical prostatectomy, brachytherapy, external beam radiotherapy.
3. Patient has access to a PC, laptop or tablet with internet connection.

Exclusion criteria are:

1. A combination of PSA ≥ 10 and Gleason = 7 (which defines high risk prostate cancer).
2. Cognitive impairment or being too ill at time of the study.
3. Insufficient understanding of the Dutch language to complete questionnaires and understand the DA.

Intervention

After being diagnosed with prostate cancer, but before a treatment decision has been made, patients in the intervention arm receive access to the online DA. Healthcare providers are instructed to introduce the DA and the study at diagnosis. However, the pragmatic nature of this trial allows hospitals to integrate the introduction of the DA with their standard information provision routines if that follows later due to follow-up diagnostics or an additional consultation with (oncology) nurses. In daily practice, this means that either the urologist or the (oncology) nurse introduces the DA to the patient. To use the DA, patients receive a card from their urologist stating their relevant disease characteristics (PSA, Gleason, and eligible treatment options) and a personal username and password to gain online access to the DA. If a nurse introduces the DA and accompanying access card, the urologist should provide the requested clinical characteristics to the nurse, either by filling in the card or by leaving a note in the patients' record.

The DA offers a stepwise guidance through the decision process. In the first step, general information about prostate cancer is provided. The second step offers the consideration between active surveillance and curative treatment (surgery or radiotherapy). Values clarification statements are presented in this step to elicit a patient's preference based on three main differences between AS and curative treatment; acceptance of deferring

treatment (*'I am confident enough that I will be treated on time, if necessary'* versus *'I do not want to postpone treatment because I do not want to be too late'*), avoiding possibly unnecessary treatment (*'If treatment might be unnecessary, I would rather wait'* versus *'I prefer treatment, even if it might be unnecessary'*) and the acceptance of treatment side effects (*'I find possible treatment side effects like erectile and urinary dysfunctions difficult to accept'* versus *'I find the possible treatment side effects acceptable'*). Each statement is related to one of the two offered treatment alternatives in this step. On a slider scale, patients can indicate for each set of statements the strength of their preference towards one of the alternatives.

Following the same structure, the next step supports the consideration between surgery and radiotherapy. For surgery, three common methods are discussed (laparoscopic, open and robot assisted). For radiotherapy this consists of brachytherapy and EBRT. Again, information provision is followed by values clarification statements. The VCMs in this step emphasize the main differences between surgery and radiation therapy (both brachy and EBRT) in terms of treatment procedure (*'I find it important that all cancer cells are removed from my body versus I find it important that the cancer cells die and not grow further'*), side effects (*'I find bowel problems worse than incontinence'* versus *'I find incontinence worse than bowel problems'*), secondary treatment (*'I am comforted by the thought that I can have radiation if surgery is unsuccessful'* versus *'I accept that surgery is difficult after radiation'*) and fear for surgery (*'I am not anxious about surgery'* versus *'I am anxious about surgery'*). If a patient already indicated a preference for active surveillance in the previous step, the program allows patients to ignore this part and continue to the last step. As a conclusion, the final step asks patients to indicate their final treatment preference and briefly explain their choice. The DA does not provide a treatment advice, but helps the patient to reach an informed preference. A summary then provides an overview of all answers to the statements and the patients' final preference. To discuss this summary with their urologist, the summary can be printed or accessed online during the next consultation.

All statements used in the VCMs were developed by a team of urologists, psychologists and engineers based on previous experience and observation of conversations where treatment decisions were discussed. The statements were evaluated during usability-testing among patients, urologists and nurses (N=10).

Recruitment

Patients in both arms will be recruited by their treating urologist. When meeting the inclusion criteria, the urologist will use a letter and leaflet, in which the study is clarified, to invite eligible patients to participate. The letter and accompanying leaflet about the

study will state that we would like to investigate the information provision and decision-making process in general, without explicitly mentioning that a DA is the subject of this study. This reduces potential bias from emphasizing that the DA is an addition to usual care, as the perception of any addition to usual care may evoke improved satisfaction on itself. It will also avoid a situation where patients in the control group feel that they are withheld from a potentially helpful tool. Patients are not informed about the randomization at the hospital level.

For all logistics involved to distributing and processing the questionnaires, the PROFILES-application will be used. 'Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship (PROFILES)' is a registry for the study of the physical and psychosocial impact of cancer and its treatment from a dynamic, growing population-based cohort of both short and long-term cancer survivors. PROFILES was developed in 2009 by a joint research group from Tilburg University and Comprehensive Cancer Centre South (CCCS) with a grant from the Netherlands Organization for Scientific Research (NWO) [31]. PROFILES enables data collection management, from inviting patients to participate in studies to collecting patient-reported outcomes data via web-based or mailed questionnaires and provides a supporting helpdesk. Patients can send their informed consent form, which they receive with the information letter, to PROFILES. On the informed consent form patients can indicate whether they want to receive questionnaires via email or regular mail. Approximately 1 to 2 weeks after treatment decision-making (T1) patients receive either the invitation (email) to fill in an online questionnaire or a paper version at their home address. In the case of a paper version, a stamped self-addressed envelope is provided to the patient to return the questionnaire. If patients do not fill in their questionnaires within two weeks, a reminder letter or email will be send. Patients will be assured that non-participation does not result in differential follow-up care or treatment. The PROFILES-application allows for managing the follow-up questionnaires, which are sent at 6 and 12 months following T1.

Outcome measures

Table 1 shows an overview of all outcome measures and the moment of measurement.

Primary outcomes

Primary outcome is decisional conflict. The decisional conflict scale (DCS) [32,33] evaluates the level of decisional conflict on five subscales; the feeling of being well-informed; the clarity of values; the feeling of support during the decision-making process; the feeling

of uncertainty about best choice; and the effectiveness of the decision. The level of decisional conflict is measured at T1. The DSC is widely accepted and applied as main outcome measure in (Pca) DA trials [24,34-36].

Table 1. Outcome measures

Outcomes	Instrument	T1	T2	T3
Shared decision-making outcomes				
Decisional conflict	Decisional Conflict Scale	X		
Decisional regret	Decisional Regret Scale		X	X
Pca Knowledge	Pca decision quality instrument	X		
Satisfaction with information	SCIP-B	X		
Decision-making preparedness	Preparation for DM-scale	X		
Decision-making role	PSDM-scale	X		
Perceived doctor-patient relationship	Single item	X	X	X
Actual treatment choice and health outcomes				
Initial preference and treatment choice	Single items	X		
Treatment satisfaction	Single item		X	X
Health-related Quality of Life	EORTC QLQ-C30	X	X	X
	EORTC QLQ-PR25	X	X	X
Side-effect impact	IIQ-7 subset for emotional state		X	X
Acceptance & Control over health status	Subjective experienced health (SBG)	X	X	X

Secondary outcomes

Secondary outcome measures can be categorized as either shared decision-making outcomes or health outcomes. Shared decision-making outcomes consist of decisional regret [37], perceived and preferred decision-making role [38], and preparation for decision-making to assess a patient's preparation for decision-making and dialoguing with his clinician [39]. Furthermore, a single-item question will evaluate the perceived patient-doctor relationship and the development of this relationship over time. Also, satisfaction with information provision [40] and knowledge [41] will be assessed.

Health outcomes refer to the actual treatment choice and any changes in treatment preference during the decision-making process. Treatment satisfaction will be measured with a single-item question: 'Are you satisfied with the way your treatment was or is executed?' To assess health-related quality of life (HRQoL) the EORTC QLQ-C30 [42] will be used. This questionnaire is developed specific to assess HRQoL in cancer patients. Much of the content of the questionnaire is appropriate for extended monitoring of health

status, including scales assessing physical, role, cognitive and emotional functioning, fatigue and sleep problems, and overall health and quality of life. This core instrument is supplemented with the prostate cancer-specific HRQoL questionnaire EORTC QLQ-PR25 [43]. This 25-item questionnaire assesses urinary, bowel and sexual symptoms and functioning, and the side-effects of hormonal treatment, though hormonal treatment is not offered as initial treatment in this study's sample. Health outcomes are further assessed by means of an evaluation of side-effect impact [44,45] and health status acceptance and subjective control [46].

Other measures

Table 2 shows an overview of the other measures. Decision aid users are asked to evaluate the DA by indicating for 25 statements if it applies to the responder or not. The first 11 statements are formulated negatively (for example 'I found the decision aid too difficult'), followed by 14 positively formulated statements (for example 'I found the decision aid pleasant to use'). Although literature reports positive effects from the usage of DAs in general [47], there may be subgroups that will not benefit from DA-usage. To identify these subgroups, additional measures on (health) skills and personality are included. Objective measures for health literacy and health numeracy are used, with the HRS Experimental numeracy module [48] and the STOHFLA-brief [49], respectively. The Decision Self-Efficacy Scale is used as a subjective measure of the perceived ability to make a decision [50].

Table 2. Other measures

Measures	Instrument	T1	T2	T3
Implementation (intervention only)				
DA-Acceptability	Self-developed	X		
(health) skills				
Self-efficacy	Decision self-efficacy scale	X		
Health numeracy	HRS Experimental numeracy module		X	
Health literacy	STOHFLA-brief		X	
Psychosocial variables				
Anxiety and depression	HADS, PC-max	X	X	X
Personality	LOT-R, BFI-10	X		
Information seeking preferences	API, NFC-short, Maximization scale	X		
Sociodemographics and other healthcare utilization		X	X	X

Comparable to health skills, the relation of personality to beneficial DA-usage will be investigated. Some studies suggest a link between personality and treatment choice [51,52]. Following these studies, some relevant aspects of personality will be taken into account: hospital anxiety and depression (HADS-scale) [53], prostate specific anxiety (MAX-PC) [54,55], optimism (Life Orientation Test – Revised) [56], the big five personality dimensions (Big Five Inventory-10) [57], information seeking preferences (subscale from the Autonomy preference index) [58] and maximization tendencies (Maximization scale) [59].

Sociodemographic variables and additional healthcare utilization

Standard sociodemographics will be asked on age, marital status, occupation, and education. Also, patients will be asked to report any additional healthcare utilization (general practitioner or other medical specialist) in the past 12 months to assess whether this affects the decision-making process.

Healthcare providers' evaluation

Healthcare providers in the intervention arm will be asked their opinion about implementation of the DA in qualitative interviews as well as questionnaires at the end of patient inclusion (approximately after 12 months). This questionnaire will be based on the MIDI-instrument [60], which is developed for the evaluation of implementing an innovation in a healthcare setting. The questionnaire will focus on usage of the DA (for example *'Did you offer the DA to all eligible patients?'*) and evaluate the pros and cons of the DA with help of statements (for example '*The DA is practical in use*'). Healthcare providers in the control condition will be asked to evaluate the current information provision and decision-making processes, their expectation of DA-usage and motivation for implementation.

Sample size calculation

The sample size for this study is determined by power analysis with decisional conflict as the primary measure. To be able to detect a clinically relevant minimum effect size [61] of .50, power is set at .80 and alpha at .05. With 19 hospitals (clusters) that agreed to participate, it is needed to estimate the intra-class coefficient (ICC). The ICC assesses the proportion of variance explained by clusters. Higher ICC values decrease effective sample size and statistical power. ICC ranges from 0 to .1 are considered common in medical literature [62]. A more specific review of ICC values in (cluster) RCTs with psychosocial measures is provided by Bell and McKenzie [63], which also included a cluster RCT evaluating a group support tool for prostate cancer patients [64]. The median estimated value for 82 longitudinal ICCs from 15 included studies was 0.0007, and the

range found for decisional conflict was between 0 and 0.02. Given the considerable variability in ICCs that is found in literature, ICC for the current trial is set conservative at 0.01.

The attrition rate is set at 25% to compensate for non-response to the questionnaires. This rate is comparable to studies in similar populations and following the same methods as this study does [65,66]. Calculations show that a design with 19 clusters of 20 patients (380 patients in total) achieves a power of .8. Taking into account a 25% attrition rate between the first and third questionnaire, the total sample size (rounded) will be set at 475 patients. This results in a recruitment of 25 patients per hospital.

Statistical analysis

All analyses will be conducted using SPSS version 19.0 (Statistical Package for Social Sciences, Chicago, IL, USA). A 0.05-significance level will be adopted in all statistical tests.

We will perform a descriptive statistical analysis of organizational (hospitals) and socio-demographic (patients) characteristics in order to assure the comparability of the intervention and control groups. Baseline measures and changes in outcome variables over the study period for each study arm will be presented as means (± SD).

The main outcome decisional conflict is measured at T1 and will be compared between both groups (intervention and control). Multilevel modelling will be carried to take the hierarchical structure of the data into account by specifying random effects at both hospital and patient level. The least square mean proportions will be estimated and compared to assess the effect of the DA on decisional conflict.

The secondary outcomes will also be compared between both groups using multilevel modelling. Some of the secondary measures consist of repeated measures (for example HRQoL and decisional regret) and will be treated according the appropriate mixed-model approach, that is repeated measures anova/ancova will be used for outcomes with two time points (decisional regret, treatment satisfaction) and a random coefficient approach will be used for outcomes with three time points (HRQoL) [67]. Observed variation in treatment choice during the trial period will be compared between groups and at level of the individual hospital. For this second comparison each hospital's particular historical treatment variation profile (2008 to 2012) will be obtained from the Netherlands Cancer Registry.

Potentially confounding variables (for example, personality, health skills, and age) will be explored for their impact on the primary and secondary outcomes. Missing data and drop-outs will be described.

Ethical considerations

The research protocol was examined by the accredited regional Medical Research Ethics Committee 'METC Brabant', and concluded that participants are not subjected to any procedure or imposed to perform any behavior. With this conclusion the obligation to fulfill the specific requirements of the Dutch law for Medical Research involving Human Subjects (WMO) was waived (reference: NW2014-03). The science committee of the initiating hospital has approved the study protocol (reference: WB/mt/14.030). All participating patients will sign an informed consent form.

DISCUSSION

This study investigates the effect of an interactive, web-based, treatment decision aid for early-stage prostate cancer. It compares impact on the decision-making process and patient reported outcomes from an intervention group with a control group. Included patients will be followed for 12 months to investigate long term consequences from the intervention on regret, treatment satisfaction and quality of life. Randomization will take place at the hospital level, meaning that once included, all patients within in one hospital receive the same treatment. Compared to randomization on the level of the patient, this design is less prone to contamination bias. The strength of this study is the initial involvement of 19 participating hospitals. With this large number, a proper variation of local circumstances can be taken into account that might affect structural adaptation of the DA in clinical practice. The large number of participating hospitals also requires careful management by the researchers during the trial period. Motivating all involved doctors, nurses and assistants requires careful monitoring of inclusion progress per location, and adaptation to specific circumstances. Another challenge is to take the treatment variation per hospital into account. If past-year treatment characteristics appear to be imbalanced between both arms, we may decide to adjust for past year treatment, based on hospital-specific treatment profiles obtained from the Netherlands Cancer Registry.

Although we are aware of the fact that individual differences between clinicians could also affect decision outcomes, there are some considerations that justify taking the institution as the unit of analysis. First, diagnosis and offered treatment plans are often the result of multi-disciplinary consideration (for example, urologists, radiotherapists,

and oncologists). Secondly, specialization often leads to some clinicians seeing the majority of Pca patients within an institution. Taking the clinician as unit of analysis could lead to too small clusters in some cases. On the other hand, clinician specialization could also lead to patients visiting multiple clinicians within a hospital before a final decision is made, making it difficult to attribute a treatment decision to a certain clinician. Third, information provision and decisional support is often provided by specialized (oncology) nurses. Typically they assist more than one clinician which could contaminate individual clinicians' data. Finally, regional variation in treatment practices, which is expected to be influenced by DAs as explained in previous sections, is generally reported at the hospital level. This indicates that there are influences at the hospital level driving practice variation that go beyond individual differences between clinicians within a hospital. The reported variation in selected treatments between hospitals is available for hospitals included in our study, though no data is available on individual clinician's variability.

While carefully designed and reviewed by experts, some content of the DA can remain the subject of discussion among healthcare providers. As every urologist, radiotherapist or nurse can be seen as an expert on prostate cancer from their own perspective; all have their own preference in formulating and presenting options, facts and risks involved to prostate cancer and its treatment alternatives. The original DA is tested thoroughly and documented for the topics that should be addressed in the DA, which we took over [23,24]. All adjustments that were made to adjust the DA to Dutch clinical setting are based on the IPDAS criteria [25] for DA development. All textual content is derived from Dutch and European treatment guidelines.

A potential limitation of our DA is that a device with internet connection is needed to use the DA, which could affect our sample and consequently our findings. Although we are aware that this could be a relevant issue in many regions in the world, we do not expect biased results in our trial. The World Bank has estimated internet access in The Netherlands is among the highest in the world, with 94% of the households (2013) having internet access (www.worldbank.org). Even in older age groups (65 to 75 years) regular internet access is at 80%, and this percentage is rapidly increasing (2013, Statistics Netherlands). Internet is routinely referred to as part of information provision in standard care. As most of our questionnaires (in both groups) are sent via email, internet access and the ability to use it is also required in both groups, assuring group comparability on this matter.

Our trial has defined decisional conflict as primary measure. As previously mentioned, the DCS is a widely accepted and applied measure in DA evaluations. However, the DCS is also subject to some discussion in the literature about its usefulness as outcome measure in DA evaluations [68]. This is mainly due to its limitation to identify a good decision as a person's underlying sensitivity to uncertainty may not be fully represented in a high or low decisional conflict score. For example, a high score on the DCS could also represent the effort that one takes to be involved in the decision-making process and absorbing all available information and therefore becoming aware of the difficulty of the decision. Although we are aware of this potential limitation of the DCS, we believe decisional conflict represents the best available affective-cognitive outcome measure that captures the uncertainty involved to prostate cancer treatment decision-making. Uncertainty about disease progression, treatment success and side-effect impact are key elements of the decision-making process in prostate cancer care. Preliminary investigations prior to the current study taught us that decisional conflict levels are substantial; we expect that our DA will be able to reduce these levels and that this potential reduction is meaningful. For meaningful interpretation of our effects we also have additional outcome measures available that can support our findings or can indicate bias if present. Many of our secondary measures focus on the decision-making process (knowledge, satisfaction with information provision, decision-making role) rather than the outcome in terms of a 'good' or 'bad' decision, this ensures that our conclusions on the usefulness of the DA will not solely depend on interpretation of the DCS.

On a broader level, this study will augment the current paucity of information regarding the implementation of DAs in (Dutch) routine clinical practice, its impact on the treatment decision-making process and long term effects. This will help patients and clinicians to establish optimal patient-treatment fit. As we hypothesized the effects could involve improved patient involvement and knowledge resulting in higher decision and treatment satisfaction and ultimately reduce regret and improve quality of life.

Finally, the results of this project will contribute to the increasing awareness of shared decision-making and improving patient centered care in the treatment of prostate cancer. This study can provide the scientific evidence needed to include the use of a DA in the prostate cancer treatment guidelines.

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Chapter 6

IMPACT OF A WEB-BASED PROSTATE CANCER TREATMENT DECISION-AID ON PATIENT-REPORTED DECISION PROCESS PARAMETERS: RESULTS FROM THE PROSTATE CANCER PATIENT CENTERED CARE TRIAL

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ABSTRACT

Purpose – To compare patients' evaluation of the treatment decision-making process in localized prostate cancer between counseling that included an online decision aid (DA) and standard counseling.

Methods – Eighteen Dutch hospitals were randomized to DA counseling (n=235) or the control group with standard counseling (n=101) in a pragmatic, cluster randomized controlled trial. The DA was provided to patients at, or soon after diagnosis. Decisional conflict, involvement, knowledge and satisfaction with information were assessed with a questionnaire after treatment decision-making. Anxiety and depression served as covariates.

Results – The levels of decision involvement and conflict were comparable between patients in both groups. Patients with a DA *felt* more knowledgeable but scored equally well on a knowledge test as patients without a DA. Small significant negative effects were found on satisfaction with information and preparation for decision-making. A preference for print over online and depression and anxiety symptoms were negatively associated with satisfaction and conflict scores in the DA group.

Discussion – The DA aimed to support shared decision making, while outcomes for a majority of DA users was comparable to patients who received standard counseling. Patients who are less comfortable with the online DA format or experience anxiety or depression symptoms, could require more guidance toward shared decision making. To evaluate long-term DA effects, follow-up evaluation on treatment satisfaction and decisional regret will be done.

BACKGROUND

In a clinical area where multiple equal effective treatments are available for the same medical condition, the preference-sensitive treatment selection that is then required can be challenging for patients as well as physicians [1-3]. Treatment selection for localized prostate cancer (Pca), the most commonly detected cancer in men in the Western world, is such an area [4]. When diagnosed at a localized stage, Pca can be managed with equal successful curative treatments (surgery or radiotherapy), or by following an active surveillance (AS) protocol without harming survival perspectives [5-8]. Although oncologically equivalent, treatments differ in their impact on quality of life, risk of side effects and perceived burden, therefore, Pca treatment guidelines do not indicate a single superior treatment option, but recommend shared decision-making (SDM) to come to the best patient-treatment fit [5, 6, 9-11]. Moreover, many Pca patients have a poor understanding of differences in treatment risks prior to choosing treatment, are dissatisfied with information received, and experience regret after treatment [12-14]. With SDM and more decision support these problems can be resolved.

SDM requires patients to share preferences, uncertainties, and the desired level of participation in the decision process. A physician should be aware of the patient's preferred level of involvement and take this into account to adequately provide all available information about eligible options, including risks, benefits and scientific uncertainties [15, 16]. However, patient preferences for involvement are often misinterpreted by care providers and many patients are dissatisfied with the information they received [17-20].

To facilitate and improve the process of SDM, patient decision aids (DAs) were developed to help patients to increase choice awareness, provide high quality information, structure the decision process, and to help clarify preferences and values [21-23]. Simple DAs are plain paper versions, while more elaborate DAs are built as interactive websites that include explicit values clarification methods [24, 25]. DA effects are typically studied by comparing patient reported outcomes following decision-making between a DA group and a usual care group. In a review of DAs across all medical screening and treatment decisions, it has been shown that DAs contribute to improved patient involvement in the treatment decision, less decisional conflict and more conservative treatment choices [26].

In the specific area of Pca treatment decision-making, DA results are less conclusive. Positive effects are seen for improved patient education (knowledge, information satisfaction), but mixed effects are found for other decision process measures such as decisional conflict [27]. Often the studied Pca DAs did not fully comply with the

International Patient Decision Aid Standards (IPDAS), mostly because of missing DA development information or unbalanced presentation of treatment benefits and risk. Furthermore, they lacked a user-centered design or were not specifically aimed at facilitating SDM in the patient-doctor encounter [27-30].

In the absence of a Dutch Pca treatment DA that included a values clarification method, a novel web-based DA was developed with a specific user-centered focus on facilitating SDM [31]. A cluster randomized controlled trial (RCT) that compared DA counseling to a control arm with standard counseling was set up. The primary finding that the DA helped patients align treatment choices to their personal preferences was published previously [32]. The current study investigated patient reported outcomes related to the decision making process, directly following treatment decision-making. We hypothesized that with the DA decisional conflict (primary outcome) would be lower and patient involvement, Pca knowledge and information satisfaction (secondary outcomes) would be better, compared to the control group [18]. Moreover, we were interested in individual differences (DA format preference, anxiety and depression symptoms) among DA users to explain potential differences in outcomes within the trial's DA arm.

METHODS

Participants and recruitment

All patients from participating hospitals, who were newly diagnosed with localized Pca (PSA <20, Gleason <8) between August 1, 2014 and July 1, 2016, had at least two treatment options and no mental or cognitive impairments, were suitable for enrollment in this trial. Patients were recruited at diagnosis by their urologist or by an (oncology) nurse immediately following diagnosis and were given a study package containing an information letter, informed consent form, leaflet and a pre-stamped envelope. To agree with participation, the informed consent form had to be returned using the pre-stamped envelope. On the informed consent form patients indicated the date of their next consultation, which usually was two or three weeks following diagnosis and the moment to discuss treatment choice. A questionnaire was sent within one week after this indicated date by email (paper version on request) [18].

Design

Eighteen Dutch hospitals were randomized to the intervention or control arm. All hospitals were general hospitals, except for one academic hospital in the control arm. Patients in the control arm received information and counseling as usual, patients from hospitals in the intervention arm received access to the online DA in addition to

usual information and counseling. Randomization at hospital level was chosen to avoid contamination of usual counseling with components of the DA. Patients were informed that the topic of the study was to evaluate information provision and treatment decision-making in Pca care, and were unaware of assignment to trial arm as the DA was not mentioned as subject of this study. The regional Medical Ethics Review Board waived the need for formal ethical approval (reference: NW2014-03), and the study protocol was approved by every individual hospital. The study was pre-registered in the Dutch Trial Register (NTR4554).

Intervention

To invite patients to use the DA, patients in the intervention arm received an access card from their health care provider with the DA-web address, and a unique username and password. The card also stated the patient's relevant clinical characteristics, that is, eligible treatment options (AS, surgery, brachy therapy, or external radiation), PSA, and Gleason score. Based on the indicated treatment options, the DA allowed patients to skip information about non-eligible treatments. After accessing the DA and entering the clinical data from the card, patients first could read general information about Pca, before detailed information about AS and treatments was provided. Provided treatment information within the DA was similar for each treatment and consisted of information about procedures, risks, and pros and cons. Information was based on (inter)national guidelines and recent scientific literature. Values clarification methods (VCMs) were included to help patients clarify their personal preference for AS or any of the treatments. VCMs were designed as statements that required a trade-off between two treatment modalities (e.g. 'If treatment might be unnecessary, I prefer to wait', as trade-off between AS and treatment). The DA ended with a summary page that displayed how extensive the DA was used (e.g. 'You have read *x* out of *x* topics'), the patient's responses to the VCMs and indicated treatment preference. A printed summary could be taken to the subsequent consultation where the treatment decision was discussed with the urologist. The goal of the summary page is to enable a SDM conversation as it presents the patient's preferences on the various VCMs and for treatment. A more detailed description of the development and content of this novel Dutch web-based DA is available in a separate publication, which also provides evidence for IPDAS compliance of the current DA [29, 31].

Procedures

In addition to usual information, patients in the intervention arm were granted access to the online DA. The pragmatic aspect of the current trial allowed hospitals to follow their existing procedures and routines for further counseling. For some hospitals this

meant that all newly diagnosed patients saw a radiation oncologist (when eligible for radiotherapy) and an oncology nurse, while at other hospitals this only happened by patient request. Most patients took two or three weeks to consider their treatment choice before a follow-up consultation was scheduled. Patients in the intervention arm received explanation that the DA should be used during this period, and that the summary provided by the DA, could be taken to the next consultation, although this was not mandatory. In the week following the treatment decision, patients in both arms were invited to fill out the questionnaire online or a paper questionnaire was sent on request. Automatic reminders were sent after two and four weeks if the questionnaire had not yet been started or completed.

Measures

Sociodemographic and clinical information was obtained from informed consent (date of diagnosis, date of birth) and the questionnaire (marital status, education level, treatment options, treatment choice, and self-administered co-morbidities). Eligible treatments and the received treatment were verified through the patient's medical record, this data was also used for a separate analyses of treatment choices within this trial [32]. Individual differences between patients in general anxiety and depression symptoms were assessed with the Hospital Anxiety and Depression Scale (HADS) [33].

Main outcome of this study was decisional conflict, which was measured with the Dutch version of Decisional Conflict Scale (DCS), incorporating five subscales regarding feeling uninformed, values clarity, perceived support, decision uncertainty and the perceived effectiveness of the decision. Scales were converted to 0 to 100, with higher scores indicating more perceived conflict [34 35]. Internal consistency of the full scale was good (Cronbachs alpha, 0.87, subscales 0.58-0.86). Secondary outcomes included two single items on the patient's perceived role during decision-making (Problem-Solving Decision-Making Scale) and the perceived preparedness to make the treatment decision (Preparation for Decision-making Scale, alpha=0.97) [36, 37]. Pca knowledge was assessed with an estimation of the perceived knowledge level per treatment (e.g. 'How well do you think your knowledge about surgery is?') and an objective test consisting of five multiple-choice test questions from the Pca Decision Quality Instrument [38]. Additionally, satisfaction with timing and format of the information received was measured with the corresponding subscale of the Satisfaction with Cancer Information Profile (SCIP-B, alpha=0.96) [39]. In the DA arm, participants received additional questions to evaluate the DA (e.g. 'Was the online DA format your preferred format?' and 'Would you preferred if the DA had provided you with a treatment advice?').

Statistical analyses

Descriptive statistics are presented as means (+/- SD) for continuous variables and frequencies and percentages for categorical variables. Differences between study arms and between responders and non-responders were tested using independent sample *t*-tests for continuous variables and chi-square analyses for categorical variables.

Analyses were performed according to the intention-to-treat principle, assuming that counseling in the DA group was different from the control group because of the introduction of the DA, regardless of actual DA usage by participants. To take the hierarchical structure of the data -due to randomization at hospital level- into account and control for hospital specific effects, linear multilevel regression analyses were used to test the effect of the intervention (the DA) compared to the control group. Study arm (DA vs. usual care) was included in the model as an independent variable. Dependent variables consisted of decisional conflict, involvement, knowledge, and information satisfaction. Participants' HADS scores served as covariate as anxiety and depression symptoms are common after receiving a cancer diagnosis and are known to be related to the evaluation of information provision [40, 41]. Subgroup analyses were performed on participants from which DA log data indicated the DA was actually used. Participants were grouped according to their DA format preference (online versus paper) and HADS score. HADS scores were initially categorized into normal (0-7), mild (8-10), moderate (11-14), and severe (≥15), according to previous studies [42]. Because differences between the mild and moderate group are of little clinical relevance, and to ensure higher statistical power, the mild and moderate categories were collapsed into one group.

The study was powered to detect a clinically relevant effect size of .50 between both study arms on decisional conflict. A conservative intra-class coefficient (ICC) of 0.01 was taken, therefore, to obtain 80% power and allow for 25% attrition in the current questionnaire and follow-ups, 238 patients per study arm were targeted [18]. Eventually, fewer patients than targeted were recruited for the control group (n=109). Due to the conservative sample size calculation, power for making comparisons between arms was still sufficient (>.80), but low for comparing smaller subgroups (.65-.67). Statistical analyses were conducted using SPSS 22.0 (Statistical Package for Social Sciences, Chicago, IL). Tests were two-sided and considered statistically significant if p<.05.

RESULTS

Based on national cancer registry data, the estimated total number of eligible patients during the trial period was 2,000 patients, of which 484 patients were invited to participate in the trial. A total of 382 Pca patients signed informed consent (DA=273 and control=109, consent rate 79%) and 336 patients filled out the post-decision questionnaire (response rate 88%). The mean age of responders was 65.3 (*SD*=5.9), there were no differences in sociodemographic or clinical characteristics in participants between both study arms (Table 1). Questionnaire non-responders were younger than responders (*M*=62.9 vs *M*=65.3, *p*=.01), although the distribution among age groups was comparable (*p*=.18; Table 2). Furthermore, non-responders were less likely to have accessed the DA compared to responders (68 vs. 86%, *p*=.005). The number of patients enrolled per hospital varied between 1 and 64 (Table 1), response rates from all hospitals except one were higher than 80% (Table 2).

Between trial arms, no differences were found on involvement or decisional conflict (Table 3). Participants in the DA arm *felt* more knowledgeable, but less prepared to make a decision (Table 3). Overall information satisfaction was lower in the DA arm, in particular for information usability, the amount of information, and completeness of the information (Table 3). The mean objective knowledge (test) scores were comparable between trial arms (Table 3), however, within the control arm, knowledge scores were lower for patients eligible for 3 or 4 treatments ($F(2, 84)=5.84$, $p=.004$), while in the DA arm, test scores were unrelated to the number of eligible treatments.

A subgroup analysis revealed that 84% of actual DA users (N=156) were in favor of the online DA format and 16% (N=30) would preferred to have received the DA in print. Of participants who received but did not access the DA, 56% (N=15) indicated a DA in print was preferred. Participants favoring the online DA format were younger (*M*=64.6 vs. *M*=67.3, *p*=.02) and more often highly educated (50% highly educated vs 27%, *p*=.04). Mean HADS scores were not statistically significantly different between both format preference groups, however, medium or severe HADS scores were more common in participants who would prefer a printed DA (*p*=.03). DA users in favor of the online DA format and with HADS scores <8 reported less decisional conflict and more information satisfaction compared to other DA users (Table 4). A treatment advice from the DA was preferred more often by DA users with severe of high HADS scores, although differences did not reach statistical significance (Table 4). No other socio-demographic variables were associated to differences between DA users. The same HADS categorization did not yield statistically significant differences in the control arm (data not shown).

Table 1. Sociodemographic and Clinical Characteristics of participants

Characteristics	Total (n=336)	DA arm (n=235)	Control arm (n=101)	*p*
Patients				
Age at informed consent, mean (SD)	65.3 (5.9)	64.9 (6.0)	66.3 (5.7)	.06
≤55, n (%)	23 (7%)	16 (7%)	7 (7%)	.09
56-65, n (%)	141 (42%)	109 (46%)	32 (32%)	
66-75, n (%)	166 (49%)	106 (45%)	60 (59%)	
≥76, n (%)	6 (2%)	4 (2%)	2 (2%)	
Marital status, n (%)				
Married/living together	295 (88%)	208 (89%)	87 (87%)	.70
Other	41 (12%)	27 (11%)	13 (13%)	
Education, n (%)				
Low	112 (34%)	76 (33%)	36 (36%)	.41
Medium	82 (25%)	54 (23%)	28 (28%)	
High	137 (41%)	101 (44%)	36 (36%)	
Gleason Score, n (%)				
6	178 (63%)	134 (61%)	44 (69%)	.25
7	106 (37%)	86 (39%)	20 (31%)	
PSA level, mean (SD)		7.9 (3.8)	8.3 (3.5)	.41
≤10.0, n (%)	253 (79%)	180 (79%)	73 (79%)	.88
10.1-20.0, n (%)	68 (21%)	49 (21%)	19 (21%)	
Number of eligible treatments				
2	74 (23%)	49 (21%)	25 (28%)	.51
3	157 (49%)	115 (50%)	42 (46%)	
4	89 (28%)	65 (29%)	24 (26%)	
Anxiety and depression, mean (SD)	7.3 (6.2)	7.3 (6.4)	7.1 (5.5)	.76
Normal (0-7), n (%)	192 (62%)	131 (61%)	61 (63%)	.77
Mild (8-10), n (%)	46 (15%)	31 (14%)	15 (16%)	
Moderate (11-14), n (%)	36 (11%)	24 (11%)	12 (12%)	
High (≥15), n (%)	38 (12%)	29 (14%)	9 (9%)	
DA usage				
Yes, n (%)	203 (86%)	203 (86%)	n/a	
No, n (%)	32 (14%)	32 (14%)	n/a	
Hospitals[1], n (%)				
1		11 (5%)		
2		1 (1%)		
3		46 (19%)		
4		28 (12%)		

Table 1. Continued

Characteristics	Total (n=336)	DA arm (n=235)	Control arm (n=101)	*p*
5		13 (6%)		
6		17 (7%)		
7		64 (27%)		
8		35 (15%)		
9		20 (8%)		
10			6 (6%)	
11			18 (18%)	
12			9 (9%)	
13			9 (9%)	
14			23 (23%)	
15			8 (8%)	
16			20 (20%)	
17			8 (8%)	
18			0 (0%)	

P-values report comparisons between the intervention arm and the control arm according to *t*-tests for means and χ^2-tests for frequencies.
Numbers may not always add up to the same *n* due to missing data (e.g. item non-response), percentages were rounded.
[1] All hospitals were general hospitals, except hospital 14 (academic)

Table 2. Comparison of questionnaire responders versus non-responders

Characteristics	Questionnaire responders (n=336)	Questionnaire non-responders (n=46)	p
Patients			
Age at informed consent, mean (SD)	65.3 (5.9)	62.9 (6.1)	.01
≤55, n (%)	23 (7%)	5 (11%)	.18
56-65, n (%)	141 (42%)	25 (54%)	
66-75, n (%)	166 (49%)	16 (35%)	
≥76, n (%)	6 (2%)	0 (0%)	
Number of eligible treatments			
2	74 (23%)	9 (21%)	.32
3	157 (49%)	26 (60%)	
4	89 (28%)	8 (19%)	
DA usage			
Yes, n (%)	203 (86%)	26 (68%)	.005
No, n (%)	32 (14%)	12 (32%)	
Hospitals[1], n (%)			
1	11 (55%)	9 (45%)	.02
2	1 (100%)	0 (0%)	
3	46 (92%)	4 (8%)	
4	28 (82%)	6 (18%)	
5	13 (81%)	3 (19%)	
6	17 (81%)	4 (19%)	
7	64 (89%)	8 (11%)	
8	35 (92%)	3 (8%)	
9	20 (95%)	1 (5%)	
10	6 (100%)	0 (0%)	
11	18 (90%)	2 (10%)	
12	9 (90%)	1 (10%)	
13	9 (90%)	1 (10%)	
14	23 (96%)	1 (4%)	
15	8 (100%)	0 (0%)	
16	20 (87%)	3 (13%)	
17	8 (100%)	0 (0%)	
18	0 (100%)	0 (0%)	

P-values report comparisons between responders and non-responders, according to *t*-tests for means and χ^2-tests for frequencies.
[1]Rows add up to 100% to represent response rates per hospital
Numbers may not always add up to the same *n* due to missing data (e.g. item non-response), percentages were rounded.
Marital status, Education level, Gleason score, PSA level, and HADS scores were not available for non-responders.

Table 3. Effects of the DA

Outcome	DA group, N=235 Mean (SD)	Control group, N=101 Mean (SD)	β	p
Involvement				
Weighing treatment pros and cons	3.3 (0.8)	3.2 (0.8)	0.25	.12
Treatment decision	3.6 (0.9)	3.5 (0.8)	0.07	.50
Preparation for decision-making	3.6 (0.9)	4.2 (0.6)	-0.55	<.001
Decisional conflict				
Full scale	23.5 (13.4)	24.1 (13.0)	-1.30	.39
Informed subscale	16.8 (16.1)	17.7 (17.1)	-1.03	.60
Values clarity subscale	30.0 (17.8)	31.8 (17.0)	-2.55	.30
Support subscale	22.4 (16.7)	21.1 (16.0)	0.07	.97
Uncertainty subscale	33.9 (23.5)	33.5 (21.2)	-0.75	.81
Effective decision subscale	16.8 (14.3)	18.4 (15.9)	-1.99	.26
Knowledge				
Objective knowledge	7.5 (2.1)	7.2 (2.0)	0.32	.30
Subjective knowledge	7.0 (1.4)	6.6 (1.5)	0.43	.01
Satisfaction with information				
Full scale	3.8 (0.8)	4.1 (0.6)	-0.25	.04
Information usability for patient	3.8 (0.9)	4.1 (0.7)	-0.35	.01
Information usability for spouse	3.7 (1.0)	4.1 (0.7)	-0.33	.02
Amount of written information	3.8 (0.9)	4.1 (0.8)	-0.37	.02
Amount of oral information	3.7 (0.9)	4.1 (0.8)	-0.36	.02
Information completeness	3.7 (0.9)	4.1 (0.7)	-0.40	.01
Information comprehensiveness	3.9 (0.9)	4.1 (0.8)	-0.14	.31
Information accessibility	3.9 (0.9)	4.1 (0.7)	-0.14	.30
Moment of receipt	4.0 (0.9)	4.1 (0.7)	-0.10	.39
Delivery method	4.1 (0.9)	4.1 (0.8)	-0.06	.58

Means and standard deviations (SD) are presented as observed in the dataset.
Beta's represent the effect of the DA compared to the control group as obtained from linear multilevel regression analyses, controlling for HADS score.

Table 4. Subgroup analysis of actual DA users in the intervention arm (N=186, missing N=17[1])

	Format preference			Anxiety and depression symptoms			
Outcome	**Online N=156**	**Paper N=30**		**Normal (0-7) N=114**	**Medium (8-14) N=48**	**Severe (≥15) N=24**	
Anxiety and depression symptoms, Mean (SD)	6.9 (6.2)	9.4 (6.9)		3.4 (2.3)	10.3 (1.8)	20.4 (3.9)	
Normal (0-7), N (%)	102 (65%)	12 (40%)	*	114 (100%)	-	-	
Medium (8-14)	35 (22%)	13 (43%)		-	48 (100%)	-	
Severe (≥15)	19 (12%)	5 (17%)		-	-	24 (100%)	
Weighing treatment pro's and cons, Mean (SD)	3.5 (0.8)	3.0 (0.5)	**	3.4 (0.8)	3.4 (0.8)	3.3 (0.7)	
Doctor-driven, N (%)	14 (9%)	4 (13%)	**	9 (8%)	4 (8%)	5 (22%)	
Shared, N (%)	74 (48%)	22 (75%)		59 (52%)	28 (60%)	8 (35%)	
Patient-driven, N (%)	67 (43%)	4 (13%)		46 (40%)	15 (32%)	10 (43%)	
Making the treatment decision, Mean (SD)	3.7 (0.9)	3.3 (0.8)	*	3.6 (0.8)	3.6 (0.8)	3.8 (0.9)	
Doctor-driven, N (%)	9 (6%)	2 (6%)	*	7 (6%)	3 (6%)	1 (4%)	
Shared, N (%)	64 (41%)	21 (68%)		54 (48%)	20 (42%)	10 (42%)	
Patient-driven, N (%)	83 (53%)	8 (26%)		53 (46%)	25 (52%)	13 (54%)	
Preparation for decision-making, Mean (SD)	3.6 (1.0)	3.5 (0.8)		3.6 (1.0)	3.7 (0.8)	3.4 (0.9)	
Decisional conflict, Mean (SD)							
Full scale	22.1 (12.4)	28.8 (13.4)	**	21.9 (11.6)	23.7 (11.9)	28.6 (18.1)	
Informed subscale	15.1(15.2)	21.5 (19.0)	*	16.5 (17.8)	14.6 (12.6)	17.0 (13.6)	
Values clarity subscale	28.1 (17.9)	38.4 (13.4)	**	28.6 (18.3)	30.7 (14.2)	33.7 (20.3)	
Support subscale	20.2 (15.1)	26.3 (17.0)	*	20.2 (13.7)	20.1 (14.8)	29.2 (22.1)	*
Uncertainty subscale	33.1 (22.2)	37.6 (25.4)		31.3 (20.8)	35.6 (21.7)	44.1 (29.9)	*
Effective decision subscale	15.9 (13.2)	22.2 (17.5)	*	15.2 (12.9)	19.0 (13.2)	21.6 (19.5)	*

Table 4. Continued

Outcome	Format preference			Anxiety and depression symptoms			
	Online N=156	Paper N=30		Normal (0-7) N=114	Medium (8-14) N=48	Severe (≥15) N=24	
Knowledge, Mean (SD)							
Objective knowledge	7.7 (2.0)	7.4 (1.9)		7.6 (2.0)	7.8 (2.2)	7.8 (1.7)	
Subjective knowledge	7.2 (1.2)	6.0 (1.7)	***	7.1 (1.4)	7.2 (1.0)	6.4 (1.4)	*
Satisfaction with information, Mean (SD)							
Full scale	3.9 (0.8)	3.5 (1.0)	*	3.9 (0.7)	3.8 (0.9)	3.5 (0.9)	*
Information usability for patient	3.8 (0.9)	3.4 (1.1)	*	3.8 (0.8)	3.7 (1.0)	3.3 (1.1)	*
Information usability for spouse	3.8 (0.9)	3.4 (1.1)	*	3.8 (0.9)	3.7 (1.0)	3.3 (1.1)	*
Amount of written information	3.8 (0.8)	3.5 (1.1)	*	3.8 (0.8)	3.7 (1.0)	3.5 (0.9)	
Amount of oral information	3.8 (0.9)	3.5 (1.0)		3.8 (0.8)	3.7 (1.0)	3.4 (1.1)	
Information completeness	3.7 (0.9)	3.5 (1.0)		3.8 (0.9)	3.7 (1.0)	3.4 (1.0)	
Information comprehensiveness	4.0 (0.8)	3.6 (1.0)	*	4.0 (0.8)	3.9 (1.0)	3.6 (0.9)	*
Information accessibility	4.0 (0.9)	3.6 (1.1)	*	4.1 (0.8)	3.8 (1.0)	3.6 (1.0)	*
Moment of receipt	4.1 (0.9)	3.7 (1.0)	*	4.1 (0.9)	4.0 (1.0)	3.7 (0.9)	*
Delivery method	4.1 (0.9)	3.7 (0.9)	**	4.2 (0.9)	4.0 (0.9)	3.7 (0.9)	*
Preferred treatment advise from DA, N (%)	49 (31%)	11 (31%)		28 (26%)	17 (37%)	10 (44%)	

Means and standard deviations (SD) are presented as observed in the dataset. *P*-values report comparisons between subgroups according to the appropriate test (i.e. *t*-tests or Anova with Bonferroni post-hoc tests for means and χ^2-tests for frequencies).

* $p<.05$

** $p<.01$

*** $p<.001$

[1] Missing due to item non-response or missing DA user data.

DISCUSSION

In this pragmatic cluster randomized controlled trial among patients with localized Pca, adding an online DA to standard counseling did not lead to different levels of patient involvement or decisional conflict in comparison to standard counseling. Patients who used the DA did feel more knowledgeable about Pca treatments but scored equally well as participants from the control group on a knowledge test. Small negative effects of the DA were found on the scales for preparation for decision-making and information satisfaction, in particular for DA users with medium or high anxiety and depression symptoms or who would preferred the DA to be in print.

With the DA, patients were provided with structured information about Pca and possible treatments. Treatment advantages and disadvantages were presented in a balanced manner, and VCMs were included to help patients establish a treatment preference based on personal values [31]. An earlier investigation into treatment choices within this trial revealed that with the current DA, the treatment decisions were more often in line with the patient's preference instead of the doctor's preference [32]. However, this did not translate into an effect on decisional conflict in the current study, with previous Pca DA studies also finding mixed results on this outcome [27] . Possibly, this is because of the nature of the concept of decisional conflict. Despite the wide use of decisional conflict as an outcome measure in DA evaluations, it has been debated whether lowering decisional conflict should actually be the desired outcome of a DA intervention [26, 27, 43, 44]. Careful consideration of all available treatment options, including weighing pros and cons against personal preferences, could evoke conflict and the perceived decision difficulty, regardless of interventions to support the decision making process. If ultimately, the final decision has a better patient-treatment fit, existence or even increase of decisional conflict could also be the expense of a thorough decision-making process [45, 46]. Follow-up evaluation of our trial participants is planned to determine if patients are more satisfied with the selected treatment and experience less regret, after treatment is completed, compared to patients from the control group.

Next to finding no effect on decisional conflict, the effects from the DA on the secondary outcomes, preparation for decision-making and information satisfaction, were small but opposite from what was expected and overall findings in DA studies [18, 26]. Although patients were unaware of randomization at hospital level and were not informed that the DA was the subject of this study, care providers were aware that the purpose of the study was to compare the DA to usual information routines. During counseling, the novelty of the DA might have been over-emphasized, increasing patients' expectations and leading to a more critical evaluation of the DA in the questionnaire. An indication

that some participants might have had other expectations from the DA was found in the proportion of patients who indicated they would like to have received an explicit treatment advice from the DA, while this was not provided by the DA.

Some evidence for an effect of the DA on knowledge was found. Firstly, participants with a DA perceived themselves to be more knowledgeable. Secondly, participants in the DA group scored equally well on the knowledge test, regardless of the number of eligible treatments, while in the control group test scores were lower if the number of eligible treatment options increased. This could indicate that when more treatments are considered, the DA helps to gain more knowledge about all options resulting in a better informed treatment decision, while in the control group there might have been more focus on a single treatment [43].

Not all participants seemed equally suited to receive the DA in its current online format. Older and lower educated participants indicated more often that a print DA was preferred over the current online format. Having internet access is common in The Netherlands, also among elderly, of all people aged up to 75 years, 97% has internet access at home (statline.cbs.nl). However, with increasing age, actual usage and comfort in using internet is lower, which could explain some hesitation among participants to engage in an online tool for making a high impact treatment decision [47]. Participants with anxiety and depression symptoms showed more decisional conflict and less information satisfaction with the DA compared to participants with similar symptoms from the control condition. Anxiety and depression is common after a cancer diagnosis [40]. However, for participants in the control condition, we did not find a moderating role of anxiety and depression symptoms on decisional conflict or information satisfaction. This could indicate that without a DA, care providers were able to tailor their counseling according to the estimated level of anxiety and depression, while with the DA, all information about risks and side-effects was presented equally explicit to all patients. Communicating uncertainty can lead to lower satisfaction, in particular if patients are more sensible to this because of anxiety or depression [45]. Further research is needed to determine if these groups require further tailored information provision or more guidance in using a DA.

The role of the DA in tailored information should be investigated in future research. During the current trial, most men received the DA soon after diagnosis, and were instructed to use the DA after consultation, regardless of any psychosocial distress from receiving the Pca diagnosis. Distress could have hindered uptake of new information from the DA and the decision-making process [48]. Possibly, some patients benefit from more extensive nurse counseling throughout the decision process and emotions caused

by the diagnosis before the DA is introduced. Detailed analysis (by audio or video) of clinical consultations could be helpful to investigate to what extent psychosocial distress plays a role during treatment counseling, and if the DA is of more added value with a tailored approach with various levels of nurse guidance [49].

A major strength of this study was the cluster randomized design to reduce the risk of contamination of standard counseling with components of the DA. Consequently, care providers in the DA arm were able to develop a routine in distributing and explaining the DA. Furthermore, many patients were recruited in the DA arm and once distributed, many patients used the DA.

Some limitations need to be mentioned as well. Firstly, recruitment of participants in the control arm was slower and resulted in less participants than aimed for. Although patient characteristics were very similar in both arms, we cannot exclude a potential selection bias in the control arm which may have led to recruiting only patients who were more likely to consent. Secondly, as mentioned before, care providers were aware of randomization and the true focus of this study. In the control arm this could have led to modifications of existing information or counseling routines due to the increased attention for SDM from this study, or in the DA group, to the creating of too high expectations as care providers could have (over-)emphasized the novelty of the DA. Thirdly, although the DA achieved a high usage rate, non-users were more likely to also not respond to the questionnaire. The evaluation of patient who chose not to use the DA are therefore underrepresented in the current sample. A qualitative study could provide more insights in their motives to not use the DA.

This study measured DA effects immediately following treatment decision-making. Previous research showed that effects from VCMs included in DAs could also emerge at a later point than at treatment decision-making [50]. Post-treatment follow-ups in the current sample on treatment satisfaction and decisional regret are needed to determine if this is also the case for this DA [18].

In conclusion, this study did not find evidence of beneficial effects from the DA on patient-reported decision process parameters. Importantly, patients who do not favor the online DA format or present with anxiety and depression symptoms could require more guidance and support during DA use and treatment counseling. The effect of the DA on treatment satisfaction and decisional regret once treatment is completed, needs to be investigated in a follow-up study.

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Chapter 7

LONGITUDINAL REGRET AND PATIENT SATISFACTION AFTER DECIDING ON TREATMENT FOR LOCALIZED PROSTATE CANCER WITH OR WITHOUT A DECISION AID. RESULTS AT ONE-YEAR FOLLOW-UP IN THE PCPCC TRIAL

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Submitted

ABSTRACT

Objective – To investigate the effect of including an online decision aid (DA) during prostate cancer treatment counseling on decisional regret and patient satisfaction in a one-year follow-up.

Methods – Eighteen Dutch hospitals were randomized to DA counseling or care-as-usual, patients (n=382) completed questionnaires directly after treatment decision making, and 6 and 12 months later. Regret was assessed with the Decisional Regret Scale, patient satisfaction consisted of satisfaction with information (SCIP-B) and treatment satisfaction. Anxious and depressive symptoms (HADS) and the perceived patient-doctor trust relation were included as possible covariates.

Results – At follow-up, regret about the choice of treatment was rare (19%) and most patients were satisfied with their treatment (91%) and the information that was received (64%) at the time of decision-making, regardless of being exposed to the DA. The perceived patient-doctor relation and anxious and depressive symptoms were associated with the odds of reporting regret and information satisfaction.

Conclusion – Including a DA in treatment counseling did not result in different decisional regret or satisfaction levels twelve months after treatment was chosen, compared to the control group.

An optimal patient-doctor relation and attention for anxious and depressive symptoms can help minimizing the risks for decisional regret and patient dissatisfaction.

BACKGROUND

Prostate cancer is the most common malignancy in men in the Western world (1, 2). When detected at an early (localized) stage, multiple curative treatments (surgery, external beam radiotherapy, brachy therapy) can be considered, or the disease can be managed by active surveillance (AS), with identical survival (3-5). The perceived burden of the treatment procedure and impact of side-effects can be different for individual patients (6-8). Reaching an optimal fit between patient and treatment is the most important goal in treatment counseling. However, many treatment decisions in Pca care tend to reflect the doctor's preference instead of the patient preference (9-11). While involving patients in the treatement decision, providing adequate information, and discussing all options reduces the risk of patients regretting their decision (12-15).

Decisional regret is defined as 'remorse or distress over a (health care) decision' (16). Up to a quarter of Pca patients are known to experience regret after choosing and undergoing treatment, which can persist up to 15 years after treatment (13, 17). In contrast to the expectation that treatment specific side-effects (e.g. incontinence after surgery) cause regret, most studies have not found differences across treatment modalities (11, 18-20).

In order to involve patients in the decision-making process and enable well-informed and preference-concordant decisions, current Pca guidelines recommend a shared patient-doctor decision (21). The use of patient decision aids (DAs) is promoted to facilitate this process of shared decision making (SDM). DAs provide balanced information on all treatments, help clarify personal values, and guide patients to establish an informed treatment preference with realistic expectations (22, 23).

Studies on the long term consequences (i.e. regret) of decisions made after DA interventions are less common. The latest Cochrane review on the effects of DAs included 7 out of 105 DA studies that reported on decision regret, of which none were in Pca patients (24). Only one of these 7 studies reported lower regret in DA users (25). Other studies that did focus on Pca patients found weak or no long-term DA effects on decision regret (26, 27). Feldman-Stewart and colleagues found beneficial effects from values clarification exercises (VCEs) included in a Pca DA on regret at a one-year follow-up, while no differences were found 3-monthts post-decision, suggesting a positive DA effect can still emerge long after the decision is made (28).

A novel Dutch web-based Pca treatment DA with VCEs has been developed and tested in a pragmatic, cluster randomized trial (29, 30). Evaluations directly after treatment choice showed that patients with the DA made different treatment choices compared

to patients from the control group, and that these treatment choices were more often driven by patient-preference rather than doctor-preference (31). However, in contrast to what was hypothesized, no beneficial effects from the DA on decisional conflict, information satisfaction, or preparation for decision-making were found immediately after treatment decision-making (32). Moreover, the DA was evaluated less positively by patients with anxious and depressive symptoms (32). Since Feldman-Stewart et al. (28) found late effects from the VCEs included in their DA, we are interested in possible long-term effects from the current DA.

Next to decisional regret, as our primary long-term outcome, we included patient-reported satisfaction with treatment and information as secondary outcome. We hypothesize that since the DA evaluated all treatment options, including their advantages and disadvantages, patients´expectations about treatment results will be more realistic, resulting in low regret and high treatment satisfaction (33, 34). Furthermore, in line with this hypothesis, and Feldman-Stewart´s finding of potential late DA effects, we aim to evaluate the DA effect on information satisfaction at follow-up.

METHODS

Design

The Prostate Cancer Patient Centered Care (PCPCC) trial was set up as a cluster randomized controlled trial, with eighteen Dutch hospitals randomized to either include the DA into treatment counseling, or to provide information and counseling as usual. Randomization at hospital level was chosen to avoid contamination of usual counseling with components of the DA. The regional Medical Ethics Review Board waived the need for formal ethical approval (reference: NW2014-03), and the study protocol was approved by participating hospitals. The study was pre-registered in the Dutch Trial Register (NTR4554) (29).

Participants and procedure

All patients newly diagnosed with localized low or intermediate risk prostate cancer (T1–T2N0M0), and a minimum of two treatment alternatives (including AS), were eligible for participation (35). Exclusion criteria were mental or cognitive impairment, or inability to complete a questionnaire in Dutch. Patients were recruited at diagnosis, and informed that the topic of the study was to evaluate information provision and treatment decision-making in Pca care. On the consent form, patients indicated the date of the subsequent consultation during which the treatment decision was planned to be finalized. The first questionnaire was sent after this indicated date (T1). Follow-

up questionnaires were sent 6 (T2) and 12 months (T3) later. Patients were unaware of assignment to trial arm as the DA was not mentioned as subject of this study. Care providers and researchers were not blinded of trial assignment (29).

Intervention

In addition to all information provided as part of usual care, patients in the intervention arm were invited by their care provider to access the DA online. The DA included information about all treatments, values clarification exercises (VCEs), and a summary that could be taken to the next consultation. Based on which treatments the patients was eligible for, the DA allowed patients to skip elements about treatments they were not eligible for (30).

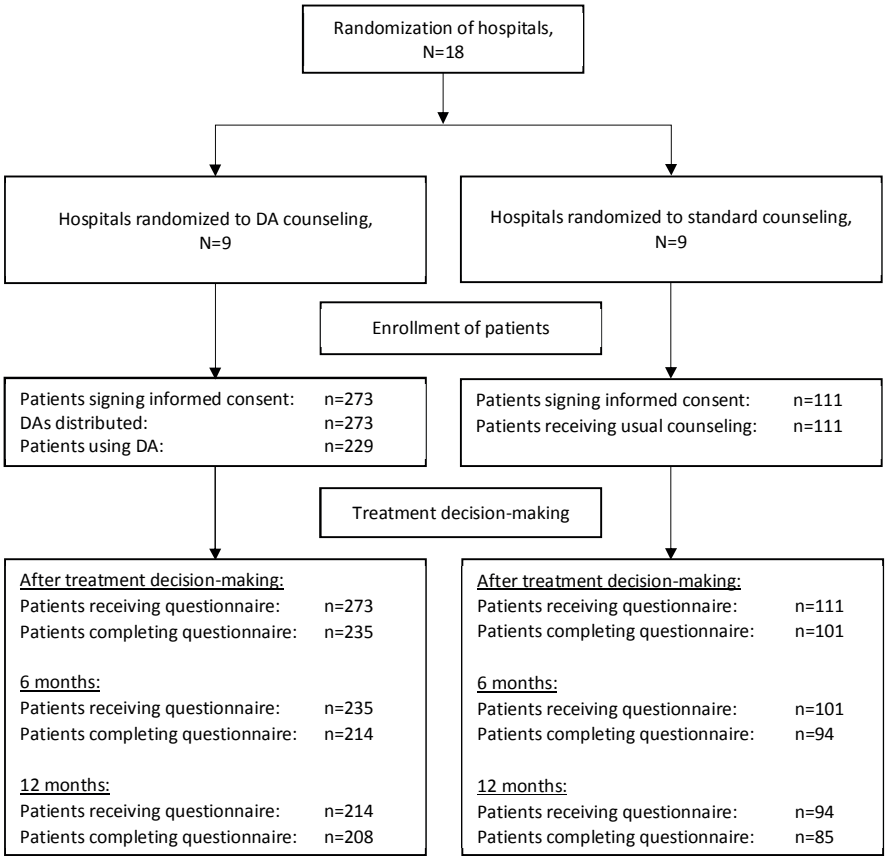

Figure 1. Flow diagram of patients included in the Prostate Cancer Patient Centered Care (PCPCC) trial

Measures

Age, marital status, and education level were obtained from the questionnaire. The treatment that was received by the patients was verified through their medical record.

Regret after the treatment decision was assessed with the five-item Decision Regret Scale (DRS) (16). All questions were answered on a 5-point scale, ranging from 1-completely disagree to 5-completely agree. Scores were transformed to a 0-100 scale. Previous studies used a cutoff score of >25 as indicative for moderate to strong regret (18, 36, 37). Regret was assessed at T2 and T3. Internal consistency was good (Cronbach's alphas 0.84-0.87). Patient satisfaction consisted of treatment satisfaction and information satisfaction. Treatment satisfaction was assessed with a single item ('Are you satisfied with how your treatment is or was executed'), to get an overall estimation of satisfaction. Since participants in our trial were exposed to different treatments, questions about specific aspects of treatment would not apply to all participants. Moreover, the single-item question contributed to limit the questionnaire length and patient burden when completing it. The question was answered on a 5-point scale, ranging from 1-completely disagree to 5-completely agree, and transformed to a 0-100 scale. Treatment satisfaction was assessed at T2 and T3. Information satisfaction was assessed with the Satisfaction with Cancer Information Profile part B (SCIP-B) (38). Answers were given on a 5 point scale, ranging from 1-very dissatisfied to 5-very satisfied, and transformed to a 0-100 score. Information satisfaction was assessed at all three time points. Internal consistency was good (Cronbach's alphas 0.95-0.97).

An earlier study into retrospective information satisfaction in Pca survivors showed that decision role preferences were associated to information satisfaction even at four years after decision-making (39). Therefore, the perceived patient role during treatment counseling, assessed at T1 with the Problem-Solving Decision-Making (PSDM) Scale, was included into our analysis as covariate (40). The PSDM scale represents the level of involvement in weighing treatment pros and cons and in making the decision, ranging from 1-passive (doctor only) to 5-active (patient only) involvement. The first two and last two answer categories were each combined, resulting in a doctor-driven, shared or patient-driven role. Furthermore, anxious and depressive symptoms were included as covariate, which are a common factor in Pca treatment decision-making, and showed an association to the DA evaluation immediately following decision-making (41, 42). Presence of anxious or depressive symptoms were assessed with the Hospital Anxiety and Depression Scale (HADS) (43). Both aspects were measured with a seven-item subscale. The answering scale ranged from 0-3, and answers were summed to obtain anxious and depressive scores. Scores ≥8 are generally seen as substantial levels of anxiety or depression (43). HADS was assessed at all three time points. Internal

consistency was good (Cronbach's alphas 0.87-0.91). To control for any changes in the overall patient-doctor relation over time, we included this variable with a single item ('How would you rate your relationship (trust) with your doctor?') at all time points, answered on a 5-point scale, ranging from 1–poorly to 5–excellent (29). The patient-doctor relation can also be a component of treatment satisfaction (44), however, in case of Pca treatment, the clinician responsible for the execution of treatment, could be different from the urologist with whom patients have their regular consultations with. Therefore, we chose to assess this variable separately from treatment satisfaction.

Statistical analysis

Intention-to-treat analysis included all patients from both arms. Descriptive statistics are presented as means (and SDs) for continuous variables and frequencies (and percentages) for categorical variables. Differences in characteristics between trials arms, and between responders and non-responders were compared with t-tests for continuous variables and chi-square tests for categorical variables.

To assess determinants of clinically relevant levels of regret and information satisfaction, scores were dichotomized with a score >25 indicating regret and <75 indicating dissatisfaction. These new variables each served as outcome variable in a multivariable logistic regression that included age, education, marital status, received treatment, trial arm, perceived role during decision-making, anxious and depressive symptoms, and the perceived patient-doctor relation as covariates. The association between these factors and the outcome variable are presented as odds ratios (with 95% confidence intervals). Statistical analyses were conducted using SPSS 22.0 (Statistical Package for Social Sciences, Chicago, IL). Tests were two-sided and considered statistically significant if $p<.05$.

RESULTS

In total, 384 patients were enrolled in this study (DA: n=273, control: n=111) and received the initial questionnaire after treatment decision-making (T1, response rate 88%). Follow-up questionnaires after 6 months (T2) were sent to 336 patients (DA: 235, control: 101, response rate 92%), and to 308 patients after 12 months (T3, DA: 214, control: 94, response rate 95%). Completion rates were comparable across participants from all hospitals. Men without a partner and men with low education were more often lost to follow-up (Table 1).

Table 1. Patient characteristics

	DA group	Control group		Complete participation	Lost to follow-up	
	N= 235	N=100	*P*-value	N=270	N=65	*P*-value
Patients						
Age at informed consent						
Mean (SD)	64.9 (6.0)	66.2 (5.7)	.06	65.6 (5.8)	64.2 (6.4)	.09
Marital Status, n (%)						
Married/together	208 (89%)	87 (86%)	.54	244 (90%)	51 (60%)	<.001
Other	27 (11%)	14 (14%)		27 (10%)	34 (40%)	
Education, n (%)						
Low	76 (33%)	36 (36%)	.41	81 (30%)	31 (48%)	.02
Medium	54 (23%)	28 (28%)		69 (26%)	13 (20%)	
High	101 (44%)	36 (36%)		117 (44%)	20 (31%)	
Gleason sum, n (%)						
6	134 (61%)	44 (69%)	.25	141 (61%)	37 (71%)	.16
7	86 (39%)	20 (31%)		91 (39%)	15 (29%)	
PSA level, mean (SD)						
≤10.0, n (%)	180 (78%)	72 (75%)	.92	203 (77%)	49 (79%)	.94
10.1-20.0, n (%)	50 (22%)	24 (25%)		61 (23%)	13 (21%)	
Number of eligible treatments						
2	49 (21%)	25 (28%)	.51	59 (23%)	21 (27%)	.74
3	115 (50%)	42 (46%)		130 (50%)	37 (47%)	
4	65 (29%)	24 (26%)		71 (27%)	20 (26%)	
Treatment received						
Active surveillance	68 (31%)	19 (19%)	<.001	63 (24%)	26 (36%)	.11
Surgery	87 (39%)	29 (29%)		98 (37%)	26 (36%)	
Radiotherapy	67 (30%)	52 (52%)		101 (39%)	21 (28%)	
Other/unknown	13	1		9	6	
Perceived role in weighing pros and cons, n (%)						
Doctor-driven	24 (10%)	16 (16%)	.23			
Shared	123 (54%)	56 (56%)				
Patient-driven	81 (36%)	28 (28%)				
Perceived role in treatment decision, n (%)						
Doctor-driven	13 (6%)	6 (6%)	.94			
Shared	104 (45%)	47 (47%)				
Patient-driven	113 (49%)	47 (47%)				

Table 1. Continued

	DA group	Control group		Complete participation	Lost to follow-up	
	N= 235	N=100	*P*-value	N=270	N=65	*P*-value
Hospitals						
1	20 (7%)		<.001	9 (3%)	6 (7%)	.26
2	1 (1%)			0 (0%)	1 (1%)	
3	50 (18%)			37 (14%)	10 (12%)	
4	34 (13%)			19 (7%)	12 (15%)	
5	16 (6%)			10 (4%)	5 (6%)	
6	21 (8%)			13 (5%)	4 (5%)	
7	72 (25%)			53 (20%)	13 (16%)	
8	38 (14%)			31 (11%)	6 (7%)	
9	21 (8%)			18 (7%)	3 (4%)	
10		6 (6%)		6 (2%)	0 (0%)	
11		20 (18%)		13 (3%)	1 (1%)	
12		10 (9%)		8 (3%)	1 (1%)	
13		10 (9%)		8 (3%)	2 (2%)	
14		24 (22%)		19 (7%)	5 (6%)	
15		8 (7%)		5 (2%)	3 (4%)	
16		23 (21%)		17 (6%)	3 (4%)	
17		8 (7%)		5 (2%)	3 (4%)	
18		Merged with hospital 14				

No differences were observed in socio-demographic- or clinical characteristics (PSA, Gleason), or the degree of involvement to the treatment decision process between participants from both trial arms. Patients in the DA group chose AS or surgery more often and radiotherapy less often compared to patients from the control group. Although it was aimed to have equal sized samples in both arms and across hospitals, fewer patients were recruited for the control group, and patient enrollment varied across hospitals (Table 1). Post-hoc power analysis revealed sufficient power at all time points (92-87% power) to detect clinically relevant differences (*d*=0.4) between trial arms at all time points, but low power (38-34%) to detect small effects (*d*=0.2).

Overall, 15% of the participants (n=57) indicated regret (with a score >25) at six, and 19% (n=43) at twelve months after treatment decision-making. But the largest proportion of men from both trial arms reported zero regret at both time points (T2: 36%, n=108, T3:

39%, n=114). Differences in regret between trial arms at both time points did not reach statistical significance (Table 2). Within the DA group, mean regret was significantly lower at T3 compared to T2 (*M*=13.5 vs *M*=17.4, *t*(179)=2.30, *p*=.02).

At both time points of follow-up, most participants were (very) satisfied with their treatment, regardless of trial arm. Information satisfaction was lower for participants from the DA group compared to the control group immediately after treatment decision-making (*M*=70.8 vs *M*=77.8, *t*(200.5)=3.02, *p*=.006), but there was no difference between trial arm groups 6 and 12 months later (Table 2). The perceived patient-doctor relation was equal across trial arms (Table 2).

Table 2. Patient reported outcomes per trial arm in the first year after treatment was chosen

	All treatment groups	
	DA N=207	**Control N=96**
Decision regret (0-100), Mean (SD)		
T2	17.4 (20.6)	13.4 (14.5)
T3	13.5 (16.9)	12.7 (15.4)
Treatment satisfaction (0-100)		
T2	80.7 (28.3)	82.6 (24.5)
T3	82.6 (21.4)	81.5 (23.4)
Information satisfaction (0-100)		
T1	70.8 (20.1)	77.8 (15.8)**
T2	76.2 (17.2)	78.5 (19.6)
T3	76.4 (17.2)	78.2 (18.7)
Anxious and depressive (0-44)		
T1	7.4 (6.5)	7.2 (5.5)
T2	6.8 (6.4)	6.1 (5.7)
T3	6.5 (5.5)	6.2 (5.1)
Perceived patient-doctor relation (1-5)		
T1	3.7 (0.8)	3.8 (0.9)
T2	3.8 (1.0)	4.0 (0.9)
T3	3.9 (0.9)	4.0 (0.9)

Note: T1 was before treatment start; treatment satisfaction and decision regret were not surveyed at this time point
P-values represent comparisons between trial arms of unadjusted means according to independent samples t-tests
* $p<.05$, ** $p<.01$, *** $p<.001$

Table 3. Factors associated with regret and information (dis)satisfaction at 12-months follow-up

	Regret			Information dissatisfaction[a]		
	OR	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
DA received			.86			.95
No	1.00			1.00		
Yes	0.94	(0.46, 1.93)		1.02	(0.52, 2.00)	
Age	1.01	(0.95, 1.07)	.74	0.99	(0.94, 1.05)	.85
Education			.11			.50
Low	1.00			1.00		
Medium	0.37	(0.15, 0.94)		0.91	(0.41, 2.06)	
High	0.71	(0.32, 1.58)		0.66	(0.31, 1.41)	
Marital status			.61			.36
With partner				1.00		
Other	0.76	(0.27, 2.16)		11.63	(0.57, 4.67)	
Treatment received			.77			.98
AS	1.00			1.00		
RP	1.94	(0.81, 4.63)		1.09	(0.50, 2.36)	
EBRT	1.22	(0.34, 4.39)		1.12	(0.36, 3.45)	
BT	1.81	(0.69, 4.72)		0.90	(0.37, 2.16)	
Perceived role in weighing pros and cons[1]			.50			.12
Doctor-driven	1.00			1.00		
Shared	1.50	(0.45, 4,97)		1.40	(0.45, , 4.37)	
Patient-driven	2.22	(0.22, 8.87)		2.95	(0.81, 10.69)	
Perceived role in decision-making[1]			.18			.23
Doctor-driven	1.00			1.00		
Shared	0.43	(0.09, 1.95)		0.57	(0.13, 2.57)	
Patient-driven	0.25	(0.05, 1.26)		0.34	(0.07, 1.64)	
Anxious and depressive symptoms[2]	1.12	(1.05, 1.26)	<.001	1.11	(1.04, 1.18)	<.001
Perceived patient-doctor relation[2]	0.35	(0.24, 0.53)	<.001	0.32	(0.22, 0.46)	<.001

OR – Odds ratio; CI – Confidence interval
AS – Active surveillance; RP – Radical prostatectomy; EBRTx – External beam radiotherapy; BT – Brachytherapy; DA – Decision aid
[a] Information satisfaction was dichotomized into 1=satisfaction <75, 0=satisfaction ≥75
[1] As assessed immediately after treatment decision-making (T1)
[2] As assessed at 12-months follow-up (T3)

In the multivariable logistic regression model (Table 3), receipt of the DA was not significantly associated with lower odds of reporting regret (OR 0.94, 95% CI 0.46-1.93) or dissatisfaction with information (OR 1.02, 95% CI 0.52-2.00) after 12 months. Participants who reported anxious or depressive symptoms or a less favorable patient-doctor relation were more likely to report regret and dissatisfaction with information at follow-up.

DISCUSSION

This study longitudinally assessed regret, as well as patient satisfaction with treatment and information received, in a sample of Pca patients who chose treatment with or without receiving an online treatment DA. Results showed that at 12-months follow-up, the DA did not significantly impact any of these outcomes. Anxious and depressive symptoms and the perceived patient-doctor relation were associated with the odds of reporting regret and information satisfaction at follow-up.

DA effects

In our study only a few men (19%) regretted their treatment one year after they made the treatment decision. This confirms previous findings in similar populations, and measured with the same scale and follow-up time (18, 24). However, in contrast to Feldman-Stewart's finding of late VCE effects (28), we did not find an effect on regret from the DA, which included VCEs, twelve months post-decision. This does not mean that the current DA or its VCEs had no effect during counseling. Patients with a DA chose different treatments compared to patients from the control condition. And as established earlier, treatment choices with the DA were more consistent with patient preferences instead of clinician preferences, while an opposite pattern is common in routine care without a DA (9, 31). With this effect established, the DA can potentially contribute to reduce unwarranted regional variations in Pca treatments (45, 46).

Decisional regret

Although no statistically significant difference in regret between trials arms was observed, a significant decline in regret within the DA arm appeared between T2 and T3. A possible explanation could be found in the larger proportion of patients who chose surgery in the DA arm. As Pca surgery has the shortest treatment time, at T2, a larger proportion of men in the DA arm was likely to have completed treatment, compared to patients from the control arm. However, surgery is also associated with severe adverse treatment effects, in particular in the first months after surgery (12, 13, 18). At T3 most

patients with active treatment were likely to have completed treatment, and patients who underwent surgery had more time to adjust, which may have resulted in similar regret levels between trial arms at T3.

Information satisfaction

Information satisfaction in the DA arm was statistically significantly lower at T1 compared to the control arm. At later time points, this difference in information satisfaction between trial arms disappeared. With the DA, information about all treatments was provided, with equal attention to the benefits and riks of each treatment. This also implied explicitly presenting unpleasant information about possible adverse treatment effects (e.g. risks, side-effects, procedures) (30). Being exposed to unpleasant information, and becoming aware that there are downsides to all treatments, could have led to lower information satisfaction in the DA group compared to the control group at T1 (47, 48). Without the DA, care providers in the control arm were able to be more implicit about risks and could adjust counseling to the level of distress in the patient. Finding similar information satisfaction scores in both arms at follow-up could indicate that eventually patients were equally satisfied with each approach.

DA implementation

The overall conclusion of little regret and high satisfaction with both treatment and information, regardless of exposure to the DA may indicate that high quality care was received by most patients in this trial. By implementing the DA we aimed to improve quality of care and stimulate SDM between patients and care providers. However, execution of SDM involves more than distribution of a DA (49). In The Netherlands, uptake of SDM in clinical routine, including Pca care, is increasing (50). An example is the opportunity to visit both a urologist and a radiation oncologist to discuss treatment options from both viewpoints. In both trials arms most patients perceived a shared or patient-driven decision, and treatment satisfaction showed a ceiling effect. In this context, the potential beneficial effects from the DA could have been too small to be picked up within the broad regret and satisfaction measures of this study. This study found that anxious and depressive symptoms and the perceived patient doctor-relation were the most relevant factors affecting regret and satisfaction at follow-up. In order to optimally utilize the possibilities to manage anxious and depressive symptoms and support the patient-doctor relation with a DA, future research should look into the best moment to introduce and use the DA. The current DA was provided to all patients directly after diagnosis and presentation of the treatment options (29). Possibly, patients with anxious and depressive symptoms require more counseling from a nurse at this stage, before new information is presented with the DA (51-53). An earlier study found a

relation between pre-diagnosis exposure to Pca treatment information and satisfaction and regret, indicating that the moment of presentation of information can have an effect on patient outcomes (27)

Future research

Relevant continuations of the current research are to investigate how the web-based aspect of the current DA is related to anxious and depressive symptoms, and incorporation of the DA into direct patient-doctor counseling. The current DA has been developed as online tool for its possibilities to tailor presentation of information (e.g. only displaying information that is relevant to the patient), include interactive VCEs, and because nearly all Dutch citizens have internet access (29, 54). As this study showed, anxious and depressive symptoms and the patient-doctor relation are associated with both regret and satisfaction. This raises the question how this relates to the fact that the DA was only available online. Use of the DA content was not integrated in clinical counseling, only discussion of the summary obtained from the DA was embedded in the follow-up consultation. Moreover, online sources could be perceived as less trustworthy, in particular for patients suffering from anxious and depressive symptoms (55-57). Possibly, these patients require offline materials that could be combined with the online DA.

The current study focused on patient-reported outcomes in the first year after treatment decision-making. A longer follow-up period (up to 36 months) including clinical data about possible tumor recurrences (or further tumor progression in case of AS) could provide insight if the patients from the DA groups adjusted better due to more accurate risk perceptions (8).

Strengths and limitations

Strengths of the current study include the pragmatic approach that allowed effects from every day clinical routine to be included in the trail, and contributing to the external validity of our results. Furthermore, drop-out rates were low and equally distributed across trial arms. Patients who consented and completed the first questionnaire were also highly likely to complete the two follow-up questionnaires.

The cluster randomized design of this trial was chosen to reduce the risk of contamination from clinicians that counsel both patients included in the DA arm as in the control arm, as in a traditional individually RCT would occur. Such design is recommended when behavior is part of the intervention (58). By taking hospitals as unit of randomization instead of patients, we avoided that care providers, after they received DA training, had

to counsel patients enrolled in the control arm as well. Moreover, randomization was blinded to patients, meaning that patients in the control arm were not aware that they were not offered an intervention. However, an important limitation of the cluster RCT may have been that it contributed to the unbalanced sampling that occurred between both trial arms. Although both arms were targeting the same number of participants, inclusion in the control arm stagnated at less then half the size of the DA arm (29). The reason could be twofold. First, after DA training, care providers in the DA arm might have been more motivated to enroll patients into the trial as they had a nove intervention to offer to patients. Second, care providers in the control arm were aware of randomization, and that the DA intervention would be compared to usual care, as provided by them. This may have caused care providers in the control arm to be more selective in which patients to enroll, consequently having an overrepresentation of more satisfied patients in the control arm and less of a representative presentation of usual care patients.

Another limitation following from the unbalanced recruitment was that for some hospitals only a limited number of patients was enrolled per treatment group, resulting in low power to detect either hospital or treatment specific effects. In particular, enrollment of patients on AS in the control group was low, leading to an underrepresentation of patients on AS in the control group.

Treatment satisfaction and the patient-doctor relation were measured with a single-item, which is generally considered to be less valid and reliable compared to multi-item measures. However, satisfaction is a construct commonly measured as a single item (e.g. in quality of life research, organization psychology, and marketing), and proving to be valid and reliable under such conditions (59-61). Existing multi-item scales to measure patient satisfaction, often include an item to assess the patient-doctor relation (44, 62) However, to answer the research questions in this study, it was preferred to obtain separate scores for both variables as the clinician treating the patient can be different from the clinician a patient has his regular consultations with. In case of follow-up studies that investigate treatment satisfaction into more detail, larger samples per treatment modality and a multi-item scale are recommended to assess more of the aspects that contribute to overall satisfaction.

CONCLUSION

Men newly diagnosed with localized Pca feel little regret twelve months after deciding on which treatment to pursue, and are satisfied with their treatment execution and the information received during treatment counseling. Receipt of an online treatment DA

did not significantly impact the outcomes at follow-up, if any, the odds of reporting regret and information dissatisfaction were associated with anxious and depressive symptoms, and a less favorable perceived patient-doctor relation. Opportunities to make the current web-based DA a more integrated part of the the patient-doctor communication should be investigated further.

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Chapter 8

ONCOLOGY PROVIDERS' EVALUATION OF THE USE OF A PROSTATE CANCER TREATMENT DECISION AID VERSUS USUAL INFORMATION PROVISION: RESULTS FROM THE PCPCC TRIAL

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ABSTRACT

Objective: To compare care providers' evaluations of an online prostate cancer treatment decision aid (DA) to an evaluation of usual information routines.

Methods: Oncology care providers (urologists and nurses, n=108) enrolled in the intervention (DA) or control (standard information) arm of a cluster randomized controlled trial were invited to fill out an online questionnaire to evaluate working with the DA or to evaluate usual information provision. Response rate was 58% (n=63).

Results: The DA was provided to 368 patients and distributing care providers were supportive of the DA content and usability. Satisfaction (1-10) with the DA or standard information was comparable (M=7.8 vs M=8.1, *p*=.14), although in the control arm, care providers perceived that patients already receive too much information. Time barriers were not expected or perceived. All care providers involved felt suitable to distribute DAs. Care providers with DA experience were more supportive of including DAs in clinical guidelines.

Conclusion: Care providers were satisfied with the DA and reported no time barriers. However, many care provider are already satisfied with standard information materials and fear to overload patients with information.

1. INTRODUCTION

To increase shared decision-making (SDM) in clinical encounters, use of patient decision aids (DAs) is recommended [1-4]. DAs come in multiple formats and, in addition to regular consultation, help to explain options, clarify values for benefits and harms, and guide deliberation and communication [5]. Studies have shown that DAs can lead to increased choice awareness, more knowledge and reduced decisional conflict [6]. Some studies even suggest patients select less invasive treatments after consulting a DA [7]. Although DAs have been developed and are available for a wide variety of treatment and screening decisions, routine use in clinical care remains limited [8].

Clinician attitudes towards SDM and DAs are an important aspect when trying to promote DA uptake [9 10]. Barriers for applying SDM were identified in earlier studies and included time constraints and perceptions that the patients or the clinical situation were not suitable for applying SDM. Identified facilitators consisted of clinician motivation, positive impact on the clinical process and patient outcomes [11]. More specific research on DA implementation showed that the method of delivering DAs to patients often is an important barrier for routine DA use. Although evidence suggests a more systematic delivery approach (e.g. automated sending though a link with the electronic patient record) is more effective compared to a clinician initiated method, clear recommendations for optimal DA delivery to patients are not yet available [8].

A clinical area in high need for SDM, and therefore ideally suited for DA use, is prostate cancer treatment decision-making [12, 13]. Prostate cancer (Pca) is the most common cancer in men in the western world [14]. Depending on patient and tumor characteristics, Pca patients could be offered a choice between surgery, radiotherapy and active surveillance. Oncological outcomes of these options are considered to be equivalent, however, each option has a specific risk and side-effect profile [15-17]. Pca treatment guidelines do not indicate a single superior option but encourage SDM to select the alternative that fits best with the patients' characteristics and preferences [18]. As SDM should include creating choice awareness, providing information about treatment harms and benefits, and preference elicitation, DAs are helpful tools to support this process.

For application in Dutch clinical care, a novel web-based Pca treatment DA has been developed and a cluster randomized controlled trial (RCT) has been conducted to evaluate patient outcomes and implementation [19, 20]. To gain insight in underlying clinician motivations for the adoption of this DA in routine clinical care, we evaluated

health care providers' experiences with the DA from the trials' intervention arm and evaluations of standard information routines and DA expectations from health care providers in the control arm.

2. METHODS

2.1 Design

In the Prostate Cancer Patient Centered Care (PCPCC) trial, eighteen Dutch hospitals were enrolled in a cluster RCT to investigate patient outcomes after implementing a Pca DA in routine clinical care compared to standard care [20]. Nine hospitals were randomized to implement the DA (intervention arm) and nine hospitals provided care and information as usual (control arm). In the intervention arm, the DA was provided to patients at diagnosis and could be further consulted at home. After usage, the DA provided a summary to discuss in the subsequent consultation with the patient's urologist. Between August 2014 and June 2016, 368 patients in the intervention arm were invited to use the DA and 136 patients were recruited for the control group to evaluate usual care. For the current study, health care providers from both arms were asked for their evaluation of routines that included either the DA or standard information practices.

2.2 Participants and procedure

One hundred and eight urologists and (oncology) nurses from both trial arms were invited to fill in an online questionnaire. The questionnaires were adjusted according to trial arm; health care providers involved in the intervention arm evaluated working with the DA, health care providers in the control arm evaluated usual information routines and were asked for their expectation about working with the DA. Questionnaires were sent a year after trial start. For the intervention arm, a minimum was required of having offered a DA to at least 15 patients. If this number was not reached within a year, questionnaires were sent when this number was achieved. As the evaluation of usual information was not affected by the number of patients included in the trial, no minimum requirements were set for this group and all questionnaires were sent a year after trial start. Reminders were sent 7 and 14 days after the first invitation.

2.3 Questionnaire

The questionnaire in the intervention arm focused on DA experiences and was based on the Measure Instrument for Determinants of Innovation (MIDI), a validated Dutch instrument designed to evaluate health innovations [21]. The MIDI questionnaire consisted

of 34 questions, grouped into four categories of factors determining implementation success; 1) instrument related factors (e.g. 'The DA provides all information necessary to work with it appropriately'), 2) advantages and disadvantages of DA use in daily routine (e.g. 'The DA makes it easier to discuss treatment options with patients'), 3) outcomes of DA use (e.g. 'DA use reduces uncertainty about treatment choice in patients'), and 4) procedural factors (e.g. 'I offer the DA to every eligible patient'). All statements were answered on a five point likert-scale ('totally disagree – totally agree' or 'never – often'). The questionnaire ended with an overall evaluation of DA satisfaction ('Overall, how satisfied are you with the DA', with 1-very dissatisfied to 10-very satisfied). All questions were in Dutch, derived from the original Dutch MIDI questionnaire and further specified to DA use [22]. The MIDI has proven to be a useful evaluation instrument in a range of Dutch studies on implementation of health innovations [23, 24]. Additional introductory questions were asked about the familiarity with the DA ('To what degree are you familiar with the DA content', with the answer scale ranging from 1-'I do not know the DA content' to 4-'I have read the DA thoroughly'), the number of patients to whom a DAs had been offered by the individual respondent (with answer categories 'none', 'between 1 and 5', 'between 6 and 10' 'more than 10') and reasons for not offering a DA to an eligible patient, with ten response categories of often reported barriers from literature (e.g., time constraints) and an open answer option.

As participants in the control arm group had no DA experience, they were only asked for their expectations on the MIDI-categories *outcomes* and *procedural factors* for when a DA would be implemented. Additionally, questions were asked about the content of usual information routines ('what is provided to patients as usual information', with seven of the most common materials as answering scale; e.g. oral information, hospital leaflets or brochures and an open field to report additional materials), health care providers' satisfaction ('how satisfied are you with the content of information patients receive in your hospital', with answers ranging from 1-not at all satisfied to 10-very satisfied) and perceived patient satisfaction with usual information ('how satisfied do you expect that patients are with the current information', with answers ranging from 1-not at all satisfied to 10- very satisfied). We also asked health care providers to estimate the information burden experienced by patients ('how do you perceive the current amount of information that is provided to patients' with answers ranging from 1-patients receive too little information to 10-patients receive too much information) and the estimated decision-making difficulty ('in general, how difficult do you expect patients experience treatment decision-making', with answers ranging from 1-no difficulty to 10-much difficulty). All participants were asked for basic demographics (gender, age, occupation and affiliation). Due to the limited number of participants per individual institution, filling in age was not obligatory to ensure anonymity.

2.4 Statistical analyses

To determine DA implementation levels per hospital, the number of patients who received a DA within the trial was compared to the absolute number of Pca patients per hospital. For continuous questionnaire data, descriptive statistics were presented as means with standard deviations (SD). Categorical data were presented as frequencies with percentages. Differences between both study arms were tested with independent sample t-tests for continuous data and chi-square tests for categorical data. Some questions allowed more than one answer and some health care providers did not answer all questions, therefore not all *n*'s always added up to the same number. All statistical analyses were conducted using SPSS version 22.0 (Statistical Package for Social Sciences, Chicago, IL, USA), and *p*-values <.05 were considered statistically significant.

3. RESULTS

Response rate was 58%, equally distributed between both arms (30/33). Responses were obtained from health care providers out of all participation hospitals, with a minimum of 2 and a maximum of 7 responders from the same hospital. Differences in gender and profession between both arms were not statistically significant (Table 1).

3.1 Intervention groups' evaluation of DA use

During the trial period 368 patients received a DAs in the intervention arm, ranging from 1 to 83 patients per hospital. Most respondents (24/29) provided DAs to patients themselves. At the moment of filling out the questionnaire, almost half the health care providers had offered the DA to a maximum of ten patients (n=15), and a third offered the DA to more than ten patients (n=10). Thirty-three reasons were reported for not offering a DA, most often because of patient characteristics (patient had already decided, refused the DA or was cognitively impaired; mentioned 15 times) or because it was forgotten by health care providers (mentioned 5 times). Most urologists (10/14) felt they were the most appropriate care provider to deliver the DA to patients, while more than half of the oncology nurses (7/12) felt equally or even more suitable for delivering the DA to patients.

Health care providers supported the DA content and working procedures; the DA was considered practical in use, the content was trusted, and DA use was not perceived to be burdensome to patients (Table 2). Mean scores on statements about easier patient-clinician conversations, clearly noticeable DA effects, and increased patient satisfaction were close to the scale midpoints (Table 2). Further, health care providers mainly indicated the DA contributed to reaching information goals (comparing treatments

options, providing insight in pros and cons), whereas preference clarification and uncertainty reduction were mentioned less frequently (Table 2). The mean overall satisfaction with the DA was 7.8 (*SD*=0.7). A large proportion of health care providers (24/29) indicated to continue DA use after the trial period.

3.2 Control groups' evaluation of usual information provision and DA expectations

A variety of information routines was reported by health care providers from the trial's control group. Verbal information and hospital specific materials were reported to be offered by all health care providers (97%). Additional information next to verbal information and hospital specific materials were not standard in all hospitals (Table 3). Patients are referred to oncology nurses for additional consultation in hospitals where oncology nurses are available, while additional consultation with a radiation oncologist is less common (indicated by 60% of respondents). Health care providers are satisfied with their current information routines (*M*=8.1, *SD*=0.9; with 1=very dissatisfied-10=very satisfied), but acknowledged that patient satisfaction with usual information might be lower (*M*=7.3, *SD*=0.7; Table 3). Only 7 respondents (23%) indicated the amount of information that patients receive is appropriate, all other respondents (*n*=23, 77%) felt Pca patients already receive too much information. On a 1-10 scale, the mean decision-making difficulty was estimated at 6.1 (*SD*=1.8; with 1=no difficulty – 10=much difficulty).

Table 1. Sample characteristics

	Total	DA group (n=30) n (%)	Usual care (n=33) n (%)	*p* value[1]
Gender				
Male	32 (51)	15 (50)	17 (52)	.90
Female	31 (49)	15 (50)	16 (48)	
Profession				
Urologist	37 (61)	15 (52)	22 (69)	.27
Oncology nurse	21 (34)	12 (41)	9 (28)	
Other	3 (5)	2 (7)	1 (3)	
Responses per hospital (min-max)	1-7	1-7	2-7	
Overall satisfaction with DA/standard information (1=not at all – 10=very much) (mean, sd)		7.8 (0.7)	8.1 (0.9)	.14

[1] Based on comparison between both study arms, according to applied t-test or chi-square test

Table 2. Evaluation of DA use in intervention arm

	DA group (n=30) Mean (SD)
DA content (1=completely disagree – 5=completely agree)	
The DA is based on factual, correct knowledge	4.1 (0.7)
The DA is based on actual knowledge	4.1 (0.6)
The information in the DA is complete	3.8 (0.7)
The DA is steering towards a certain treatment choice	2.4 (0.9)
Procedural (1=completely disagree – 5=completely agree)	
It is clear to me which activities should be executed in what order	4.2 (0.7)
The DA offers all information needed to work with	3.8 (0.7)
The DA is too complicated for clinicians to work with	2.4 (1.1)
The DA fits with standard workflows	3.9 (0.6)
I have insufficient trust in the DA	2.2 (0.8)
The DA is suitable for all patients with localized Pca	3.6 (1.1)
Using the DA saves me time	2.7 (0.8)
Patient outcomes (1=completely disagree – 5=completely agree)	
Effects from using the DA are clearly noticeable	3.2 (0.5)
Using the DA is stressful to patients	2.1 (0.6)
Activities (1=never – 5=always)	
Indicating all treatment options, each with their pros and cons	4.7 (0.5)
Indicate for which treatments patient is eligible	4.8 (0.5)
Indicate where to find relevant information	4.2 (0.9)
Stimulate patient to weigh pros and cons	4.7 (0.5)
Offer the DA to all eligible patients	4.2 (1.0)
Ask for patients' preferences	4.3 (1.1)
When needed, further explain the DA	4.2 (1.1)

Expectations on DA outcomes by health care providers in the control group did not differ from experiences by health care providers in the intervention group (Table 4). Both groups evaluated information goals (comparing treatments, provide insight in pros and cons, actual DA usage) slightly higher than patient outcomes (satisfaction, uncertainty, clarifying preferences), although differences did not reach statistical significance. Time constraints during consultation were not perceived nor expected from DA use. While health care providers in the intervention group felt DA implementation had a good fit with guidelines (M=4.0, SD=0.3), health care providers in the control group were more neutral about DA use being incorporated in treatment guidelines (M=3.1, SD=1.0, p<.001; Table 4).

Table 3. Control groups' evaluation of standard information routines

	Usual care (n=30)
Current information to Pca patients (n, %):	
Verbally	29 (97)
Hospital specific materials	27 (90)
Brochures from patient or professional association	18 (60)
Referral to website	19 (63)
The 'Prostate book'1	15 (50)
Another DA	13 (43)
Patient group meetings	1 (3)
Other	3 (10)
Standard referral to (n, %):	
Oncology nurse	26 (87)
Radiation oncologist	18 (60)
How satisfied are you with current information practices? (1=not at all – 10=very much) (Mean, SD)	8.1 (0.9)
How satisfied do you expect patients are with current information practices? (1=not at all – 10=very much) (Mean, SD)	7.3 (0.7)
How do you perceive the current amount of information to Pca patients (1=patients receive too little information – 10=patients receive too much information) (Mean, SD)	7.0 (0.8)
How difficult do you expect patients find treatment decision-making? (1=no difficulty – 10=much difficulty) (Mean, SD)	6.3 (1.8)
DA expectations (1=completely disagree – 5=completely agree) (mean, SD)	
Patients better understand information about illness and treatments	3.7 (0.5)
Patients will value clinicians' advice less	2.4 (0.8)
Patients will be better prepared to ask questions	3.9 (0.6)
It will be easier to discuss what matters most to patients	3.7 (0.7)
The DA should be offered by a urologist	2.9 (1.0)
Patients will have a more active role in treatment decision-making	3.5 (0.6)

[1] The 'Prostate book' is distributed for free by a pharmaceutical company to all Dutch hospitals

Table 4. Comparison of clinicians' experiences versus expectations of DA use

	DA group experience (n=29)	Control group expectations (n=26)	*p* value[1]
Procedural (1=completely disagree – 5=completely agree) (mean, SD)			
The DA is (would be) practical in use	3.8 (0.5)	3.5 (0.9)	.10
The DA makes (would make) it easier to discuss treatment options with patients	3.4 (0.6)	3.7 (0.7)	.11
The DA fits (should be part of) guidelines and procedures	4.0 (0.3)	3.1 (1.0)	<.001
Time constraint (n, %)			
Shorter consultations	1 (4)	2 (8)	.76
Equally long consultations	25 (86)	22 (84)	
Longer consultations	3 (10)	2 (8)	
Information goals (1=completely disagree – 5=completely agree) (mean, SD)			
Comparing treatment alternatives	4.0 (0.4)	3.7 (0.7)	.08
Provide insight in treatment pros and cons	4.1 (0.5)	3.9 (0.6)	.24
Patients actually using the DA	3.7 (0.5)	3.6 (0.6)	.34
Patient outcomes (1=completely disagree – 5=completely agree) (mean, SD)			
Reduce uncertainty about treatment choice	3.7 (0.6)	3.9 (0.5)	.43
Increase satisfaction with information received	3.8 (0.5)	3.7 (0.6)	.24
Clarify patient preferences	3.8 (0.5)	3.8 (0.6)	.93

[1] Based on comparison between both study arms, according to applied t-test or chi-square test

4. DISCUSSION AND CONCLUSION

4.1 Discussion

To increase understanding of health care providers' opinions about DA use and standard information routines, this study surveyed health care providers who were involved in a cluster RCT that compared a novel online Pca treatment DA to standard information routines. Care providers who were randomized to the trial's DA group and used the DA in clinical practice, were positive about the DA content and recommended continued use after the trial. Time was not expected nor perceived as a barrier for DA use by care providers from both groups. In the control group we found health care providers to be equally satisfied with standard information routines, although they acknowledged that satisfaction might be lower for patients and the amount of information provided to patients could be too much.

Models on successful implementation of health innovations emphasize the facilitating role of positive patient outcomes [11, 21, 25]. The intended goal of DAs is to increase knowledge, help clarify personal values and to help patient take a more active role in the process of treatment selection [5]. For the particular DA used in this study, it was already found that treatment choices made with the DA were more often in line with the patient's preferences compared to preferred option by the clinician [26]. Nevertheless, this study indicates that healthcare providers from both groups did not have strong experiences or expectations about patient outcomes after DA use. Health care providers answered items related to these aspects most often around the scale midpoints. This could indicate two potential barriers for DA implementation; first, care providers could be insufficiently aware of patients outcomes associated with DA use, and secondly, patient outcomes could be insufficiently observable by care providers at the moment of treatment decision making.

To revolve both issues, care providers should be made more aware of the potential benefits associated with DA use. Once implemented, care providers could be motivated to continue DA distribution by receiving structural feedback on DA usage rates and patient outcomes (e.g. knowledge, satisfaction with decision, and regret). This should also take into account that effects may emerge long after the decision was made (e.g., one year post-decision), requiring long-term follow-ups [9, 27].

In contrast to earlier studies, this study showed that time constraints were not perceived by health care providers who worked with the DA nor expected by health care providers from the control arm [11, 28]. Possibly, this is the result of the growing awareness and interest for SDM and DAs in recent years [29-31]. More awareness for DA use could have adjusted our respondents' expectations about consultation length when using DAs. Moreover, three major clinical trials with different Pca treatment DAs have been conducted recently in The Netherlands, with involvement of almost half of all Dutch hospitals in one of these trials and thus increasing scientific and public attention for DA usage [20, 32, 33]. This may have contributed to our finding that time constraint is not considered a barrier for DA use in Dutch Pca care. It has to be noted that care paths in Dutch Pca care already allow for multiple contact moments needed to facilitate SDM and DA use (e.g. choice talk, option talk, decision talk), whereas for DA use in other diseases or conditions some of these moments need to be added [34].

We found that the number of patients who received a DA varied widely between hospital sites. The majority of respondents in this study indicated when a DA was not offered to an eligible patient, this was because it was forgotten or the clinician estimated the patient was not suited or willing to use a DA which could potentially be a misinterpretation

of patient preferences [35]. In our study we did not make use of automated systems to distribute the DA (e.g. automated sending though a link with patient record), although some studies suggested a system-based delivery method is potentially most successful [8]. Automated systems could help recognizing eligible patients with a lower risk of forgetting or misinterpreting patient preferences to use a DA.

Furthermore, our study found mixed views on whether a DA should be introduced by a urologist or an (oncology) nurse and if DA distribution should be part of formal treatment guidelines. In this study, both urologist and oncology nurses felt themselves suited to distribute the DA. When this responsibility is not clearly defined in a local hospital's care path, a diffusion of responsibility could emerge that hinders sustained DA implementation.

Another potential barrier for DA implementation in Pca care is that health care providers in our control arm reported high levels of satisfaction with their existing (hospital specific) information materials and verbal information provision. Although health care providers in the current study acknowledged that patient information satisfaction might be lower compared to their own satisfaction, this might even be an overestimation of actual patient satisfaction. Previous studies showed that considerable proportions of Pca patients are dissatisfied with information received and that large discrepancies exist between actual information preferences and their physician's perceptions [36, 37]. This difference between actual and perceived information satisfaction could lead to reluctance among health care providers to use externally developed tools such as DAs. It is therefore important to inform health care providers about patients' actual (information) needs, but also to provide the opportunity to adapt the DA to hospital specific materials that care providers already feel satisfied with.

Some limitations of this study need to be mentioned. First, the current trial increased awareness for applying SDM in Pca treatment decision-making and for DAs in both study arms. Moreover, other Pca DAs initiatives were enrolled in a large number of Dutch hospitals as well [32, 33]. It can therefore not be assumed with certainty that no individual patient from the control group came into contact with any of the available DAs. However, we do not expect a significant effect on our results from this potential contamination, as no DAs were actively implemented in the hospitals from our study's control group.

A second limitation is the fact that DA use in this study was linked to the RCT, meaning that patients who were provided with the DA, were also asked to take part in the RCT and fill out three questionnaires. Discussing the DA with a patient therefore always

coincided with explaining the trial as well, which could be experienced as an additional burden by health care providers. Moreover, when health care providers distributed a low number of DAs this could be because they were unsupportive of DA use or because of low involvement with the trial. Potentially, those less involved health care providers could also have been less likely to fill out the questionnaire for this study. This holds the risk that the opinion of these health care providers are underrepresented in this study.

4.2 Conclusions

Health care providers who implemented the DA in clinical practice supported content and usability. Expectations on the effects of DA use were mainly related to improved information practices and less often to other patient outcomes. This could point at unawareness among care providers about common DA effects. More training and feedback on DA usage could be needed to educate care providers about possible DA effects. Importantly, this study disconfirmed time constraints as a barrier for further implementation. Health care providers reported high satisfaction with usual information, in particular hospital specific and own oral information, and fear of providing too much information. Distributing a DA through an external source could therefore be an implementation barrier. A single optimal mode of DA delivery was not identified in this study, both urologists and (oncology) nurses feel suited to distribute DAs to patients.

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Chapter 9

UPTAKE AND USAGE OF AN ONLINE PROSTATE CANCER TREATMENT DECISION AID IN DUTCH CLINICAL PRACTICE: A QUANTITATIVE ANALYSIS FROM THE PCPCC TRIAL

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ABSTRACT

Implementation of patients decision aids (DAs) in routine clinical care is generally low. This study evaluated uptake and usage of a novel Dutch web-based prostate cancer (Pca) treatment DA within the Prostate Cancer Patient Centered Care trial (PCPCC). From an estimated total patient sample 1,006 patients, 351 received a DA (35% implementation rate; hospital ranges 16-84%). After receipt of the DA, most patients accessed the DA, utilized most functions, although not completely, and discussed the DA summary in a subsequent consultation with their care provider. Including nurses for dissemination of DAs seemed to positively affect DA uptake. Once received, patients seemed able to use the DA and engage in SDM as intended, however, DA uptake and complete usage of all DA components should be further improved. Prior to the diagnosis consultation, handing out of the DA should be prepared.

BACKGROUND

When diagnosed with localized prostate cancer (Pca), patients can face a choice between multiple surgical and radiotherapy options, or decide not to be treated immediately by following an active surveillance (AS) protocol. In the absence of a generally superior treatment option, patient preferences should guide this treatment selection process [1-3]. When such a preference-sensitive health decision has to be made, a collaborative approach from both the patient and care provider is preferred to select the best suiting treatment [4]. In this process of shared decision-making (SDM) a doctor provides all relevant information about the disease, treatments and consequences, and the patient shares his preferences and concerns [5].

SDM can be initiated or enhanced with help from decision support tools, such as decision aids (DAs). DAs come in multiple formats (e.g. booklet, web-based), but all provide structured and balanced information about the disease, available treatments, and the risks and benefits associated with these treatments [4, 6]. Often, DAs also include values clarification exercises (VCEs) to elicit patient preferences [7]. Previous studies have shown that patients, after using a DA, have more knowledge, lower decisional conflict, and more accurate risk perceptions [8]. If VCEs are included, patients are also more likely to select a treatment that is consistent with their values [8].

While many trials have reported beneficial patient outcomes after the use of decision support tools, routine use of such tools in clinical care still is low [9]. Only a few examples are known of sustained DA use after their initial evaluation in a clinical trial [10, 11]. Studies that have evaluated DA implementation from a care providers' perspective identified important barriers, such as limited confidence in the (content of the) tools, time pressure and concerns about disrupting work procedures [9, 12]. A common patient-reported barrier is the feeling of being unable to engage in SDM or to use a DA, rather than being unwilling to do so [13].

Recently, policy makers in The Netherlands adopted SDM and DAs in their effort to improve quality of care [14]. Funding programs are encouraging SDM and usage of DAs. As such, patient groups, professional bodies, health care insurers and hospitals are stimulated to implement DAs for multiple medical conditions, and DA developers are stimulated to develop new DAs [15]. Although much is known about attitudes, barriers and facilitators towards SDM and DAs, there is limited data available about actual achieved degrees of implementation and the precise proportion of patients using DAs once distributed. Often this is because the tool or patient population does not allow for detailed registration of the exact number of eligible patients, number of tools

distributed or monitoring of actual usage. For example, leaflet DAs could be distributed in waiting room areas, and in such circumstances it is unknown who takes them. For an online DA that is publicly available, it is often unknown which visitors are actually patients facing a treatment decision at that particular moment. Moreover, if a DA is used in multiple hospitals, and detailed information on actual uptake and usage is lacking, less can be learned from local best practices.

A novel web-based Dutch Pca treatment DA, which was investigated in a cluster randomized controlled trial, allowed for structural monitoring of DA uptake and usage in a quantifiable patient population [16]. Therefore, this study aimed to improve understanding of the implementation results by comparing the DA uptake across hospitals and the actual usage of the DA and its elements (e.g. VCEs) by patients.

METHODS

Study sites

Eighteen Dutch hospitals agreed to participate in the trial, and after randomization, the DA was implemented in nine Dutch hospitals. The other nine hospitals formed the control arm and delivered care as usual [17]. One academic medical center participated in the trial, which was randomized into the control arm. All other hospitals were teaching hospitals. Two hospitals that were involved in DA development (before randomization) were randomized by pure chance into the intervention arm. Randomization was performed by an independent statistician, blind to hospital names [17]. The hospitals involved offered either one (AS) or two treatments (AS and surgery or radiotherapy) at their own location. Referral to another hospital for specific treatments is common in The Netherlands. Implementation started in August 2014 and data collection ended in January 2016. The need for ethical approval was waived by the regional medical ethics committee (reference: NW2014-03).

Implementation/delivery method

All urology departments of the hospitals enrolled in the trial's DA group were visited by the researchers and received an explanation of the purpose of the RCT. The DA was presented to the medical staff and the proposed method of delivery was explained. The explanation included that the DA would be introduced to patients in addition to the presentation of standard information. Depending on local work routines, the DA would usually be introduced by the urologist at diagnosis or by an oncology nurse during consultation following diagnosis. Next to the DA, patients received all information and materials (e.g. hospital brochures) that would also have been provided otherwise.

Patients accessed the DA with an individual access code that was provided to them on a card by their care provider. On that card, the care provider also indicated which of the treatments covered by the DA (AS, radical prostatectomy, brachytherapy, and external beam radiotherapy) were eligible for the patient. For gathering DA user data, receiving the post-questionnaire, and combining DA user data and questionnaire data, patients signed informed consent. The DA could be used by patients regardless of trial participation and consent, DA usage was then still monitored, as this was anonymized data not linked to individual patients.

Decision aid

The DA is in Dutch language and available online-only after login (http://prostaat.keuzehulp.nl). After accessing the DA, patients are presented with general information about Pca and treatments first. Based on the treatments available to the patient, detailed information is then provided about all treatments. Information about treatments is broken up into a section about active surveillance versus treatment, and a section about survery versus radiotherapy. Per section, values clarification exercises (VCEs) are included to elicit patient preferences for treatment. These VCEs are presented as tradeoffs between treatment attributes. The DA ends with a summary of all indicated preferences, including a treatment preference. The DA summary can be printed and brought to the following consultation with their clinician, or re-accessed online, to enable a shared patient-doctor conversation about aspects relevant to the patient. The development process and DA content (including examples of the VCEs and DA summary page) have been described in more detail before [16].

Data collection and patient questionnaires

For this study, data was gathered on the number of DAs provided by healthcare providers and the usage of the DA by patients. As the DA was provided as part of a RCT, both healthcare providers and patients signed informed consent. Study numbers on the informed consent forms were hospital specific and linked to the DA access codes. An informed consent signed by a healthcare provider represented a DA being provided to a patient; actual patient use of the DA was monitored by means of log files. Data from the questionnaires were linked to DA user data based on study number. Patient characteristics from informed consent were saved separately from the DA user data to ensure anonymity.

To determine the degree of implementation, information on the total number of eligible Pca patients per hospital was obtained from The Netherlands Cancer Registry (NCR) for a five year period (2009-2013) prior to the start of DA implementation. All

participating hospitals allowed the NCR to provide us with data about their number of patients diagnosed, except for one. From these registry data, an estimation was made on the expected number of eligible Pca patients during the trial period. Eligibility was defined as being diagnosed with low or intermediate risk Pca (PSA level below 20 and a maximum Gleason score of 7) [18]. Additionally, patients were required to have access to the Internet and to be able to read and understand Dutch language.

An online questionnaire to evaluate DA usage by patients, was sent (paper version on request) to patients after the treatment decision was made. The questionnaire included items about when the DA was received and from who (urologist or nurse), whether the DA was sufficiently explained, and whether the DA summary was discussed during a subsequent consultation.

Data analysis

The degree of implementation was calculated by dividing the number of DAs provided to patients (based on access cards distributed by care providers) by the estimated total number of eligible Pca patients (based on national registry data) per hospital. Descriptive statistics were presented as means (and SDs) for continuous variables and frequencies (and percentages) for categorical variables. Group comparisons between DA users and non-DA users and between questionnaire responders and non-responders were made with *t*-tests for continuous variables and chi-square tests for categorical data. Statistical analyses were conducted using SPSS 22.0 (Statistical Package for Social Sciences, Chicago, IL). Tests were considered statistically significant if $p<.05$.

RESULTS

From national registry data, it was estimated that during the trial period, 1,006 patients were diagnosed with localized Pca in participating hospitals. With 351 DAs distributed to patients, the average achieved degree of implementation across all study locations was 35%, varying between 16% and 84% across hospitals. Highest implementation levels (84 and 79%) were achieved in hospitals who were also involved in DA development. Implementation did not succeed in one hospital due to a lack of organizational support (also no registry data were obtained for this hospital), this hospital was therefore excluded from further analyses. Detailed implementation results across all participating hospitals is presented in Table 1.

Table 1. DA uptake per study site

	A	B	C	D		E	
Study site	**Estimated total number of Pca patients in trial period[1]**	**Number of DAs provided[2]**	**Degree of implementation (B / A)**	**Number of DAs accessed[3]**	**As % of DAs provided (D / B)**	**Number of DA summaries discussed[4]**	**As % of DA users among questionnaire responders (n=193)**
Hospital A*	99	83	84%	76	92%	43	78%
Hospital B	121	63	52%	42	67%	21	62%
Hospital C*	71	56	79%	51	91%	21	72%
Hospital D	196	45	23%	34	76%	20	83%
Hospital E	149	26	17%	20	77%	9	69%
Hospital F	81	25	31%	19	76%	11	65%
Hospital G	152	25	16%	20	80%	4	44%
Hospital H	137	24	18%	16	67%	7	64%
Hospital I[5]	n.a.	1	n.a.	1	n.a.	1	n.a.
Total	**1006**	**351**	**35%**	**279**	**79%**	**137**	**71%**

[1] Estimation based on average number of Pca patients diagnosed per individual hospital between 2009-2013, as obtained from The Netherlands Cancer Registry (NCR).
[2] Based on number of information packages with DA and informed consent distributed by care providers in trial period (2014-2016).
[3] Number of unique patients accessing DA (=DA users) (DA log data).
[4] As indicated in patient questionnaire.
[5] Not included to determine degree of implementation.
* Hospitals involved in DA development

Table 2. Self-reported sociodemographic and clinical characteristics of sample

	Questionnaire responders (*n*=235)			Questionnaire non-responders (*n*=38)		
	using DA (*n*=203)	***not* using DA (*n*=32)**	***P* value**	**using DA (*n*=26)**	***not* using DA (*n*=12)**	***P* value**
Age[1] (mean, SD)	65.0 (6.0)	64.6 (6.0)	.71	61.8 (6.8)	64.2 (4.5)	.28
Marital status[2] (n, %)						
Married/with partner	182 (90%)	26 (81%)	.23	n/a	n/a	
No partner	21 (10%)	6 (19%)		n/a	n/a	
Education[2] (n, %)						
Low	61 (31%)	15 (47%)	.12	n/a	n/a	
Middle	46 (54%)	8 (25%)		n/a	n/a	
High	92 (46%)	9 (28%)		n/a	n/a	
PSA[2] (mean, SD)	7.9 (3.8)	7.9 (4.3)	.99	n/a	n/a	
<10 (n, %)	158 (79%)	22 (76%)	.86			
10-20 (n, %)	42 (21%)	7 (24%)				
Gleason[2] (n, %)						
6	124 (64%)	10 (40%)	.02	n/a	n/a	
7	71 (36%)	15 (60%)		n/a	n/a	
Number of eligible treatments[1] (n, %)						
2	41 (21%)	8 (26%)	.41	2 (9%)	5 (42%)	.02
3	97 (49%)	18 (58%)		14 (61%)	7 (58%)	
4	60 (30%)	5 (16%)		7 (30%)	0 (0%)	

[1] Retrieved from informed consent completed by the care professional
[2] Retrieved from questionnaires
n/a = not available
Columns do not always add up to same total due to item non-response or missing data.

Table 3. DA reception and completion

	DA reception[1], n (%)				DA completion[2], n (%)				
					Step 1: AS vs treatment (n=106)		Step 2: surgery vs radiotherapy (n=277)		
Study site	**Received DA from a nurse**	**Received DA <1 week from diagnosis**	**Received no or insufficient explanation about DA**	**Would preferred paper DA instead**	**Read all information**	**Completed all VCEs**	**Read all information**	**Completed all VCEs**	**Indicated a treatment preference**
Hospital A	4 (7%)	46 (78%)	7 (12%)	11 (19%)	25 (71%)	25 (71%)	11 (57%)	14 (18%)	58 (76%)
Hospital B	28 (67%)	31 (74%)	4 (10%)	11 (26%)	5 (63%)	5 (63%)	25 (52%)	10 (21%)	28 (67%)
Hospital C	6 (18%)	26 (77%)	5 (15%)	6 (27%)	18 (72%)	15 (60%)	28 (57%)	13 (27%)	32 (63%)
Hospital D	6 (23%)	16 (62%)	3 (12%)	7 (27%)	6 (50%)	7 (58%)	19 (54%)	9 (26%)	24 (71%)
Hospital E	0 (0%)	9 (64%)	2 (14%)	2 (14%)	6 (50%)	5 (42%)	12 (55%)	2 (9%)	12 (60%)
Hospital F	5 (29%)	13 (76%)	2 (12%)	3 (18%)	2 (100%)	1 (50%)	12 (60%)	7 (35%)	14 (74%)
Hospital G	2 (20%)	8 (80%)	3 (30%)	0 (0%)	4 (57%)	5 (71%)	13 (65%)	5 (25%)	14 (70%)
Hospital H	3 (27%)	5 (46%)	2 (18%)	3 (27%)	3 (60%)	4 (80%)	9 (50%)	6 (33%)	14 (88%)
Total[3]	**54 (25%)**	154 (74%)	28 (15%)	46 (22%)	69 (65%)	67 (63%)	163 (59%)	66 (24%)	197 (71%)

[1] As indicated in patient questionnaire
[2] Retrieved from DA log file data
[3] Hospital I (N=1) is excluded

From all patients (N=351) receiving a DA, 277 patients accessed the DA (79%; Table 1). Age did not significantly differ between DA users versus non-DA users (65.2 vs 65.6, p=.60). A larger proportion of non-DA users was lower educated, but differences in education level between DA users and non-users did not reach statistical significance. The DA was used more often by patients with a Gleason grade 6 tumor (usage rate 92%), compared to patients with a Gleason grade 7 tumor (usage rate 83%, $c^2(1, N=220)=5.18$, $p<.02$; Table 2).

DA log file data showed that of 106 patients eligible for AS, 69 patients (65%) read all information about the comparison between AS and treatments, and 163/277 (59%) completed the section about surgery and radiotherapy (all DA users were eligible for at least one of these treatments). The VCEs after the first step (AS versus treatment) were fully completed by 67 of 106 eligible DA users (63%), and after the second step (surgery versus radiotherapy) by 66/277 (24%). A treatment preference was indicated by 197 DA users (71% of all DA users). Usage of the DA elements was consistent among patients from different hospitals (Table 3).

The post-decision making questionnaire was sent to 273 patients who gave informed consent (consent rate 78%) and was filled out by 235 respondents (response rate 86%). Questionnaire responders were more likely to have also used the DA (usage rate 86% vs 68%, $c^2(1, N=273)=7.81$, $p<.01$), and where slightly older (62.5 vs 64.9, $t(271)=-2.29$, p=.02) compared to non-responders. Marital status, educational level, PSA level and Gleason score were collected with the questionnaire and therefore not available for non-responders (Table 2). The flow diagram of patients included in this study is presented in Figure 1.

From the questionnaire responders who used the DA (N=193), 137 responders (71%) indicated that the summary obtained from the DA, was discussed with their urologist in a subsequent consultation (Table 1). Most respondents indicated that the DA was received within a week from diagnosis (154/208, 74%), and 158 respondents (85%) felt the DA was sufficiently explained (28 respondents indicated no or insufficient explanation was received). One out of four patients received the DA from an (oncology) nurse in, ranging between hospitals from 0 up to two out every three patients. In all other occasions, the DA was received from the urologist. A majority of the questionnaire responders (163/209, 78%) indicated that the online format of the DA also was the preferred format, 46 responders (22%) would have preferred a paper DA instead (Table 3). Figure 2 presents a flowchart of the most common workflow for DA dissemination across participating hospitals.

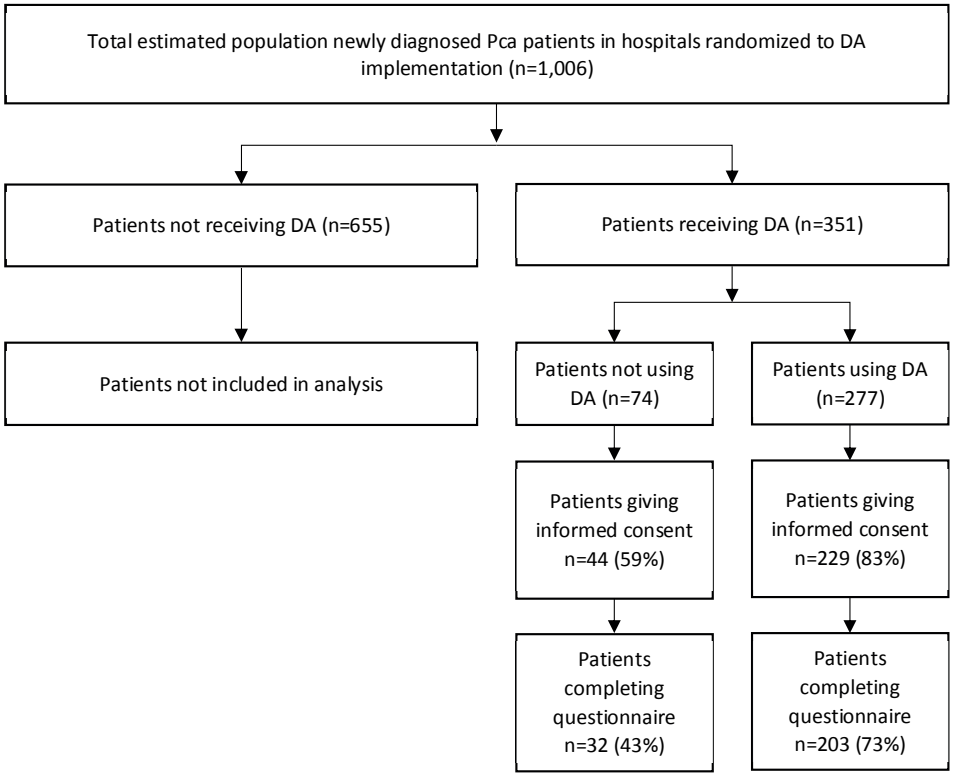

Figure 1. Flow diagram of patients included in the Prostate Cancer Patient Centered Care (PCPCC) trial.

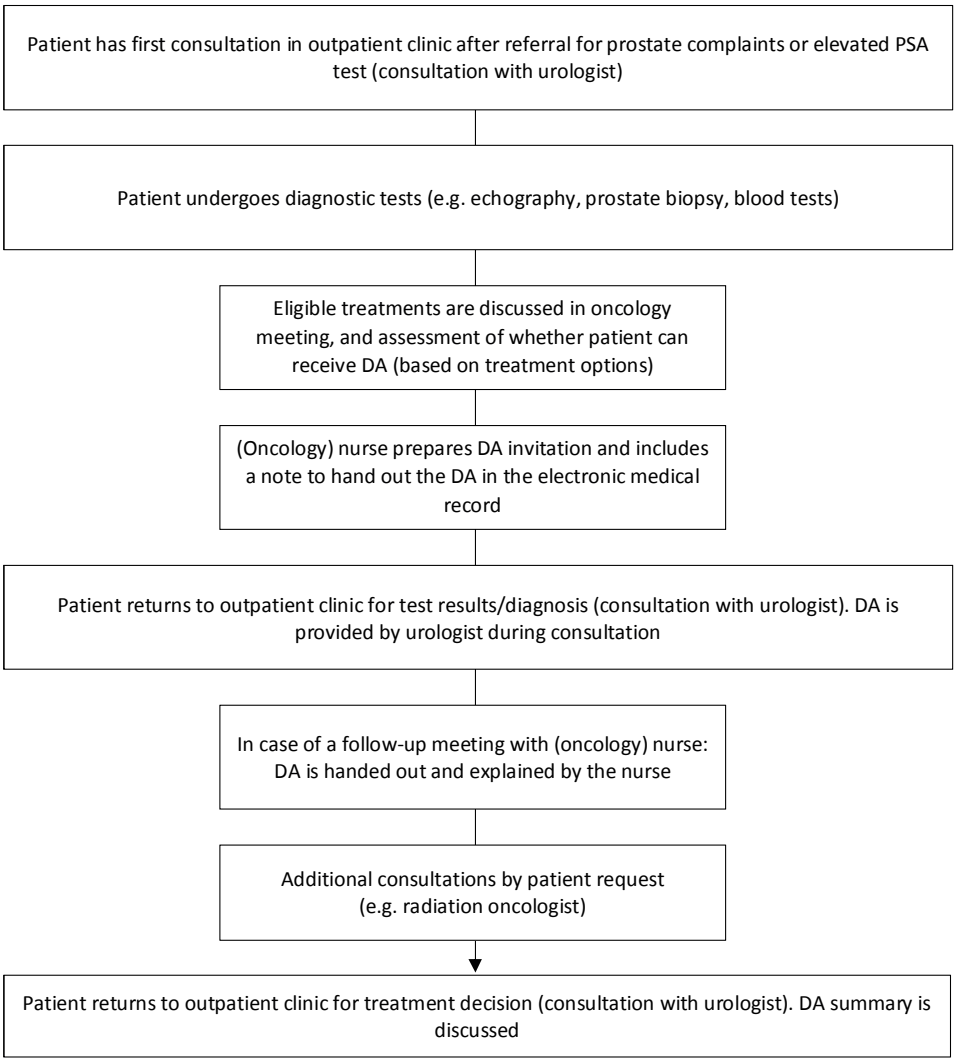

Figure 2. Flow chart of most common workflow for DA dissemination in participating hospitals

DISCUSSION

This study structurally evaluated implementation of a web-based Pca treatment DA in nine Dutch hospitals. All hospitals included the DA as part of their information routine following Pca diagnosis. On average, one in every three newly diagnosed Pca patients received a DA, but large differences were observed in implementation rates per hospital. Once a DA was distributed, most patients accessed the DA, indicated a treatment preference, and discussed the summary obtained from the DA with their urologist.

Implementation was highest in hospitals of care providers who were also involved in the development of the DA, and by random assignment enrolled in the intervention arm. Involvement during DA development may have increased intrinsic motivation to implement the DA. This motivational approach is identified as an important driver for implementing change in health care and applied in other DA development processes as well [19, 20]. To increase intrinsic motivation for care providers from institutions who were not involved in the DA development, it could be useful to offer opportunities to become more involved with the DA. For example, customization of the DA to match hospital layout, as well as the possibility to integrate the DA with existing hospital materials could improve adoption of the DA by care providers in other hospitals.

Most patients received the DA from their urologist within the first week after diagnosis and felt that the DA was sufficiently explained to them. In most hospitals the role of nurses in this process of distributing DAs was limited. In an earlier study among care providers we found that nurses and urologists consider themselves equally suitable to provide patients with a DA, and that distributing DAs should not be an exclusive clinician task [21]. Therefore, overall implementation could be further improved if nurses become more involved in the process of distributing DAs. As in hospitals that implemented best, nurses either prepared DA distribution prior to the diagnosis consultation, or handed out the DA themselves in a subsequent follow up consultation (Figure 2).

Respondents with a Gleason grade 6 tumor used the DA more often compared to respondents with a Gleason grade 7 tumor. Gleason scores provide a prognosis of oncological outcomes; a Gleason 6 score (or lower) represents the most favorable condition [22]. Consequently, patients with a Gleason grade 6 more often had all four available treatment options to choose from, while the choice set of eligible treatments for patients with a higher Gleason grade 7 tumor, was often reduced. Choosing from a smaller choice set can be perceived as less difficult, resulting in a different information

search behavior compared to patients who need information about more options [23-25]. Therefore, the DA could have been perceived as less needed by patients with a Gleason grade 7 tumor.

DA users differed in the amount of information that they read and which VCEs they answered within the DA. This could indicate that DA users differed in their information needs or did not fully understand how to navigate within the DA. However, in the questionnaire, a large majority of responders (both DA users and non-DA users) felt the DA was sufficiently explained and in previous usability tests, easy navigation was confirmed [16]. It is therefore more likely that the DA was used for specific information, beyond the information that was already known from other sources. The selective answering of VCEs could be because patients were undecided on the VCEs that were not answered, or instead, already had a clear treatment preference and did not feel the need to provide an explicit answer to the VCEs. This is confirmed by the large majority of DA users who were able to indicate a treatment preference. Follow-up research is needed to determine if the degree of DA completion has led to differences in patient reported outcomes (e.g. information satisfaction and regret).

A majority of DA users indicated that the DA summary was discussed with their clinician in a subsequent consultation. The summary reported the patient's VCE responses and treatment preference. With such a summary on paper during consultation, patients were encouraged to overcome the barrier of feeling unable to engage in SDM [13]. To further stimulate SDM in routine clinical care and engage patients and care providers in discussing preferences and values, distribution of the DA among eligible patients should be further optimized. One way to increase delivery could be to automate DA delivery, for example by having the electronic medical record automatically signal if a patient should receive a DA [26]. Alternatively, eligibility for the DA could be included as part of the multidisciplinary team meeting, where all newly diagnosed patients are discussed, and in the preparation of the consultation (e.g. 'did the patient already receive a DA?').

A major strength of this study is that it is one of the first to analyze DA implementation in a structured manner, with data on every step from DA distribution to treatment choice (number of DAs distributed, log file data on DA usage, and a post-decision evaluation). This study covers a largely neglected area in (Pca) DA implementation studies, that is, actual DA usage data [27]. Our results showed that implementation of DAs should not only be evaluated based on the number of distributed DAs, but require a more thorough investigation of the distribution procedures (e.g. role of nurses) and usage of specific DA elements (e.g. VCEs completed).

A limitation of the current study was that distribution of the DA was linked to trial participation measuring the DA's effectiveness [17]. Next to introducing the DA, care providers also had to explain enrollment in the trial and had to obtain informed consent to have patients participate in the questionnaire study. Although patients were informed that the DA could also be used without participation in the trial, it could have served as a barrier for DA use for some patients. Also, determination of the total number of eligible patients was estimated based on the number of Pca patients registered in the Netherlands cancer registry in previous years (2009-2013). Regional trends (hospital mergers, changes in offered treatments) could potentially have caused some inaccuracy in the estimation of the number of patients during the trial per hospital. Nevertheless, as these number are fairly stable over time it is unlikely that this would have a large influence on our findings. Moreover, the estimation was based on tumor stage only (cT1 and cT2), which could mean that the registry data included patients that would not have met the DA inclusion criteria due to comorbidities or other clinical characteristics. Therefore, the calculated degrees of implementation could underestimate actual implementation slightly. This, however, is likely to occur in all hospitals and could therefore contribute to a margin of error within the estimation that is equal for all hospitals and as such, is unlikely to explain variations in implementation rates observed across hospitals.

Conclusion

While many studies have provided evidence that DAs can be effective tools to support SDM in clinical practice, this study is one of the first to provide a detailed analysis of the implementation results and usage rates of a DA in clinical routine. Eight out of nine hospitals involved in this study succeeded to implement a novel Dutch web-based Pca treatment DA in clinical routine within the trial period. Uptake between these hospitals varied from incidental to structural and patients varied in the extent to which they utilized all DA components. Most patients expressed a treatment preference and used the DA summary to talk about values and preferences with their urologist. Based on our results, strategies to further improve DA adoption by care providers and patients can be targeted more specifically.

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Chapter 10

INTRODUCING DECISION AIDS INTO ROUTINE PROSTATE CANCER CARE IN THE NETHERLANDS: IMPLEMENTATION AND PATIENT EVALUATIONS FROM THE MULTI-REGIONAL JIPPA INITIATIVE

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ABSTRACT

Objectives: To assess implementation rates after multi-regional implementation of three different prostate cancer treatment decision aids (DA) in The Netherlands and patient-perceived barriers and facilitators to use a DA.

Patients and Methods: In total, 33 hospitals were asked to implement a DA in their routine care and to participate in this implementation study. Implementation rates for each DA were calculated per hospital. After treatment choice, patients (n=1,033) completed a survey on pre-formulated barriers and facilitators to use a DA.

Results: Overall implementation of the DAs in all hospitals was 40%. For each DA, implementation varied largely between hospitals from incidental (<10% of eligible patients receiving a DA) to high rates of implementation (>80%). All three DAs were evaluated positively by patients, although the concise and paper DAs yielded higher satisfaction scores compared to an elaborate online DA. Overall, patients were most satisfied when they received the DA within a week after diagnosis. The pre-formulated barriers to DA usage were experienced by less than 10% of the patients, and most patients confirmed the pre-formulated facilitators.

Conclusion: Overall implementation rate of the DAs in clinical routine was 40% and a wide variation in uptake across hospitals was observed for each DA. Most patients were satisfied with the DA they received. Sustained implementation of DAs in clinical routine requires further encouragement and attention.

INTRODUCTION

Prostate cancer (Pca) is the most common malignancy diagnosed in men in the western world. In case of localized prostate cancer, patients are typically required to choose between multiple equivalent treatment options. Although survival perspectives with each treatment are similar, treatment procedures and risk for side-effects vary, and many patients have poor understanding of these differences between treatments [1]. Therefore, clinical guidelines concerning localized Pca suggest a shared patient-doctor decision to incorporate patient preferences and values into the treatment decision [2-5]. Decision aids (DAs) have been developed to assist patients and care providers with shared decision making (SDM) [6].

Evidence for the beneficial effects of applying DAs is widely available and shows that patients have better knowledge of the treatment options, and are more aware of their personal preferences and values [7]. As a consequence, DAs help patients to take a more active role in the decision-making process [8]. So far, most DA trials, including those related to Pca treatment, focused on determining the DA effects, with limited attention for implementation aspects [7, 9]. Many DA trials took place within a single institution or location, and even if the absolute number of the DAs distributed was known, their relative reach within the targeted patient population often remained unknown [10, 11]. Moreover, uptake of DAs in daily routine, outside of clinical trials, is low, resulting in limited knowledge about successful DA implementation at a large scale [7, 12-17].

After distribution of the DA to eligible patients, the next step in implementation is actual DA use by patients. Patient-perceived barriers and facilitators related to DA usage, have been studied more extensively [13, 18-22]. Common barriers against DA usage from the patients' perspective are insufficient trust in the DA quality or its benefits, the DA being unpractical in use, inadequate timing (e.g. the DA being offered too late after diagnosis) or inadequate explanation of how to use the DA. Patient-perceived facilitators include that the DA is practical in use, and that the presented information is complete and trusted [13, 18-22].

With the current implementation study, we aimed to investigate the implementation rate of these three DAs in routine Pca care in the Netherlands, and aimed to identify possible barriers and facilitators from the patients´ perspective. This study was conducted by the Joint Implementation Prostate cancer Patient-centered care (JPPPA) consortium, consisting of three DA research groups that each developed a DA for Pca patients.

PATIENTS AND METHODS

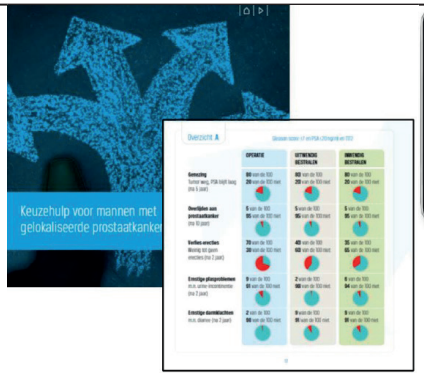
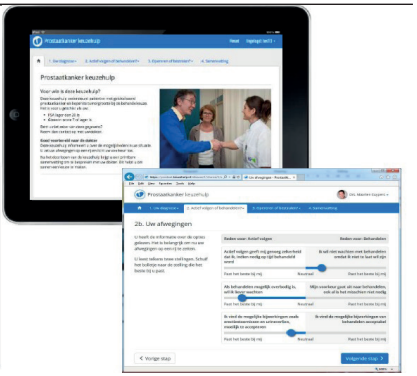
The three decision aids

Each of the three DAs involved was developed according to the International Patient Decision Aids Standards (IPDAS) and contained information about the disease, treatment options, and (dis)advantages of all options based on (inter)national guidelines and international literature [23]. Patients, urologists and radiation oncologists were involved in the development and review process of the DAs [24-26]. In each DA, the same choice options were presented: surgery, brachytherapy, and external beam radiotherapy, as well as the option of active surveillance. The DAs varied in their format and length. DA1 was a concise booklet (14 pages), DA2 was an even more concise (in diagram style with short explanations) booklet or online DA (by patient choice), and DA3 was an elaborate online DA with values clarification exercises (VCEs). The DA format coincided with the intended moment of use. DA1 and DA2 aimed to be used within consultations, while DA3's intended use was outside consultation. The characteristics of the DAs are presented in Table 1. Detailed descriptions of the separate trials investigating the DA effects have been published earlier [24-27].

Setting and participants

Thirty-three hospitals (out of a total of 90 hospitals in The Netherlands) implemented one of the three DAs in treatment counseling. Each DA was implemented in a specific region of The Netherlands (DA1 – East; 8 hospitals; DA2 – North-West: 16 hospitals; DA3 – South: 9 hospitals). Per DA, hospitals were recruited to participate based on convenience (e.g., distance), allocation of DAs to hospitals was not randomized. The DAs were handed out to patients newly diagnosed with localized Pca. For all 3 DAs, patients were eligible to participate if they had the possibility to choose between at least two treatments covered by the DA. Assessment of whether the DA was applicable (e.g. eligibility for at least two treatments covered by the DA) was done by the patient's urologist. Actual distribution of the DA was done by either the urologist or a specialized nurse, depending on what best fitted with existing local care pathways. After the treatment decision was made, but before treatment started, patients received a questionnaire to evaluate receipt and usage of the DA. All data were collected between July 2013 and June 2016. Research protocols from each DA group were reviewed by their respective local institutional ethics committees, which each provided a waiver for further ethical assessment.

Table 1. Characteristics of the three DAs

	DA 1	DA 2	DA 3
			
Implementation period	July 2013-July 2014	March 2014- March 2016	August 2014- June 2016
Number of hospitals	8	16	8
Number of DAs distributed	284	273	351
Number of patients evaluating DA	255	183	235
DA format	Print booklet	Print booklet or online (by patient choice)	Online
Intended use	During consultation	Outside consultation	Outside consultation
DA content	General information about (treatment of) Pca is described first, then specific information on the procedures, the likelihood of cure and side effects in the urinary, bowel and sexual domain for the each treatment is described. Risk information on the probabilities of progression, survival and side effects (urinary, bowel and erectile) are presented by means of pie charts. No explicit values clarification exercises are included.	Treatment options are described in short terms. Arguments in favor and against each treatment are presented separately. Pros and cons that are presented include the following topics; cure, treatment, and quality of life. No explicit values clarification exercises are presented. An alphabetical glossary of difficult terminology is included, adjusted to low literacy. No values clarification exercises are included.	Elaborate information (text and graphics) about Pca and common terminology is provided. Active surveillance is compared to treatments, and in a next step, surgery is compared to radiation options. Advantages, disadvantages, and risks of each option are discussed. Risks are presented in a graphical display. VCEs are included as statements to trade off treatment attributes. A DA summary can be obtained for use during a follow up consultation.

Outcome measures

Our primary outcome measure was the implementation rate. This rate was calculated by the proportion of patients who received a DA compared to the estimated total number of eligible Pca patients per hospital during the period the DA was implemented. Since the total number of eligible patients was not prospectively registered in a structured manner in all participating hospitals, an estimation was based on hospital-specific registry data of the six years prior to the current project, retrieved from the Netherlands Cancer Registry.

After a treatment decision was made, a questionnaire was used to collect self-reported data about patient's demographic variables (age, marital status, having children and educational level). Evaluation measures consisted of DA distribution procedures (e.g. 'Who presented the DA to you?'), DA user-friendliness (e.g. 'Did it occur fonts were too small?'), and a 24-item list of barriers and facilitators for DA use (e.g. 'I had insufficient trust in the DA') based on literature [22] (items presented in Table 3). All three DA groups used the same questionnaires to evaluate DA use in order to enable combined data analyses.

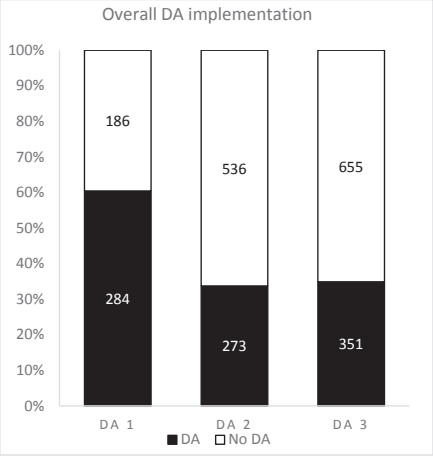
Data analysis

Descriptive questionnaire data are presented as means (*M*s) with standard deviations (*SD*s) for continuous variables, and frequencies and percentages for categorical variables. Comparisons between DAs for continuous variables were made with analyses of variance (ANOVA) and Bonferroni post-hoc tests and with chi-square tests for categorical variables. Statistical analyses were conducted with SPSS 22.0 (Statistical Package for Social Sciences, Chicago, IL). Tests were two-sided and considered statistically significant if $p<.05$.

RESULTS

During the study period, 908 newly diagnosed Pca patients received a DA out of an estimated total of 2,285 eligible patients, resulting in an overall implementation rate of 40%. With each DA, high implementation levels (>80%) were achieved in 1 or 2 hospitals, whereas for the other hospitals implementation varied considerably (2-80%). Highest average implementation was achieved with the concise paper DA1 (60%), average implementation levels for DA2 and DA3 were comparable (34-35%). Implementation rates across hospitals for each DA are presented in Figure 1.

Out of the 908 patients who received a DA, 673 patients (M_{age}= 65.7, SD=6.0) agreed to complete the post-decision questionnaire evaluating DA use (response 74%). Compared to participants from both other DA groups, participants from DA3 were slightly younger and more often highly educated (Table 2). Mean PSA and Gleason scores were lower for participants from DA3, but the same distribution across categories was found between DA groups (Table 2).



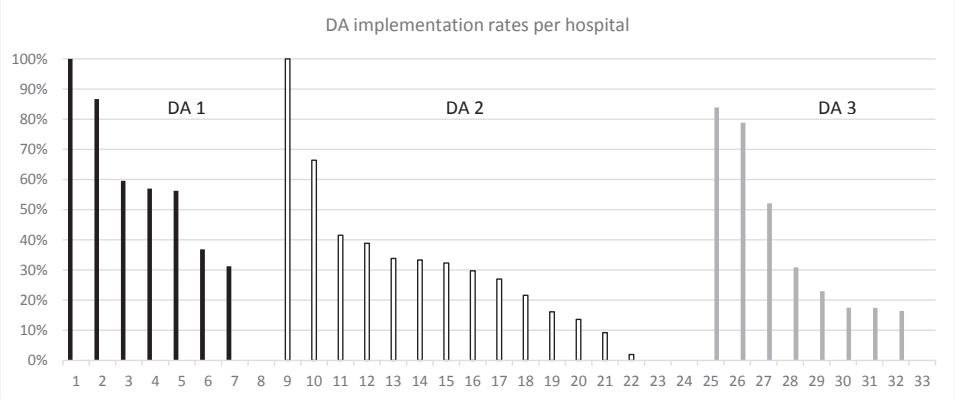


Figure 1. Implementation rates per hospital

Most participants indicated that they received the DA from their urologist (n=478, 71%) and perceived that the urologist is the most suitable person to hand out a DA (n=511, 76%; Table 3). However, of the participants who received the DA from a nurse (n=192, 29%), 60% considered the nurse to be the most suitable person for this (data not shown).

Barriers against DA usage were reported by less than 10% of the participants, regardless of which DA they received (Table 3). Differences found between DAs, were related to format (unpractical, insufficiently adjusted to personal preferences) or subjective evaluations (no confidence, expected no benefit). Overall, most barriers were reported for the elaborate online DA3.

Facilitators for DA use were reported by a large majority of participants (Table 2). For all DAs, more than 80% of participants found the DA pleasant to use and well organized and were confident in the DA quality. Overall, facilitators were reported mostly by respondents who used the most concise DA (DA2) and least by patients who used DA3. A full overview of the responses to perceived barriers and facilitators for all DA formats is presented in Table 3.

Table 2. Sociodemographic and clinical characteristics of questionnaire responders

	DA 1 (n=255)	DA 2 (n=183)	DA 3 (n=235)	*p*
Age at informed consent, mean (SD)	66.0 (5.9)	66.3 (6.2)	64.9 (6.0)	.04
Marital status, n (%)				
Married/living together	222 (87%)	149 (81%)	208 (88%)	
Single/Other	33 (13%)	34 (19%)	27 (12%)	
Education, n (%)				
Low	94 (37%)	64 (35%)	76 (33%)	.008
Medium	62 (25%)	66 (36%)	54 (23%)	
High	96 (38%)	53 (29%)	101 (44%)	
Gleason score, mean (SD)[1]	6.5 (0.7)	6.6 (0.9)	6.4 (0.8)	.05
≤6, n (%)	158 (63%)	90 (56%)	134 (61%)	
≥7, n (%)	93 (37%)	71 (44%)	86 (39%)	
Missing, n	4	22	15	
PSA level, mean (SD)[1]	9.2 (5.3)	9.9 (8.3)	7.9 (3.9)	.002
≤10.0, n (%)	183 (73%)	110 (68%)	180 (77%)	
10.1-20.0, n (%)	60 (24%)	42 (26%)	49 (21%)	
≥20.1, n (%)	8 (3%)	9 (6%)	5 (2%)	
Missing, n	4	22	1	

P-values report comparisons between trials for the control groups and DA groups, according to *t*-tests and analysis of variance (ANOVA) for means and χ^2-tests for frequencies.
Numbers may not always add up to the same *n* due to missing data (e.g. item non-response), percentages are rounded.
[1] Scores of participants from DA 1 and DA 2 were obtained from medical records, DA 3 presents self-reported scores.

Table 3. Patient DA evaluations

	DA 1 N= 255	DA 2 N=183	DA 3 N=235	*p*
Practical implementation, agreed with statement, n (%)				
Received DA from doctor	189 (78%)	138 (76%)	**151 (64%)**	.003
Doctor is most suitable to provide DA	200 (82%)	143 (81%)	**168 (72%)**	.02
Received DA within a week from diagnosis	175 (69%)	**159 (87%)**	154 (66%)	<.001
Satisfied with moment of receipt	232 (92%)	173 (95%)	196 (92%)	
DA was sufficiently explained	226 (89%)	161 (88%)	186 (87%)	
Satisfied with DA format	250 (99%)	176 (96%)	**168 (79%)**	<.001
DA added much to other information	181 (83%)	141 (83%)	**107 (56%)**	<.001
Implementation barriers confirmed, n (%)				
Forgot to use the DA	6 (2%)	4 (2%)	9 (4%)	
DA was too difficult	7 (3%)	3 (2%)	10 (5%)	
DA was steering towards a treatment	21 (9%)	14 (8%)	20 (10%)	
DA was unclear	5 (2%)	9 (5%)	12 (6%)	
DA was unpractical	10 (4%)	9 (5%)	**25 (12%)**	.002
Was not confident in DA	20 (8%)	8 (4%)	24 (12%)	.03
Expected no benefit	15 (6%)	15 (8%)	**29 (14%)**	.01
Expected DA would be burdensome	12 (5%)	4 (2%)	11 (5%)	
Not motivated to use DA	11 (5%)	4 (2%)	13 (6%)	
Expected DA would increase uncertainty	17 (7%)	5 (3%)	13 (6%)	
DA was insufficiently adjusted to specific needs	30 (12%)	**8 (4%)**	28 (14%)	.006
Implementation facilitators confirmed, n (%)				
DA was pleasant to use	223 (91%)	166 (91%)	**166 (80%)**	.001
DA was well organized	234 (95%)	172 (94%)	**175 (85%)**	<.001
DA enabled treatment comparisons	222 (90%)	164 (90%)	**163 (79%)**	.001
DA gave insight in treatment (dis)advantages	226 (92%)	170 (93%)	**168 (81%)**	<.001
Felt DA information was complete	204 (84%)	154 (84%)	**154 (74%)**	.02
DA was important addition to other information	217 (90%)	166 (91%)	**152 (73%)**	<.001
Pleasant to use DA as additional source of information	231 (94%)	160 (87%)	165 (80%)	<.001
Confident in DA quality	231 (94%)	170 (93%)	**170 (82%)**	<.001
Expected DA would reduce uncertainty about decision	167 (69%)	**146 (80%)**	124 (60%)	<.001
Used the DA to determine treatment	176 (72%)	153 (84%)	123 (59%)	<.001
DA made easier to talk with relatives	202 (83%)	160 (87%)	**129 (62%)**	<.001
DA made easier to talk with care providers	196 (81%)	157 (86%)	**123 (59%)**	<.001
Recommend DA to others	219 (100%)	171 (99%)	**172 (90%)**	<.001

Percentages are calculated based on item response, not as a proportion of the group total presented in table header.
P-values represent the outcomes of chi-square tests comparing all three DAs, significant differences caused by a single DA are indicated in bold.

DISCUSSION

Many DA initiatives struggle to get structurally embedded in clinical routine, despite ample evidence revealing the benefits of using DAs when making medical decisions [7, 13]. At the onset of a multi-regional implementation initiative of three new Pca treatment DAs in Dutch clinical practice, a consortium was formed to jointly measure implementation rates and patient evaluations (i.e., barriers and facilitators from the patients' perspective) from these three DAs. Overall, 40% of eligible Pca patients received a DA. For all DAs alike, implementation was quite successful (implementation rate >80%) in a limited number of hospitals, whereas uptake varied widely at other sites (2-80%). Overall, patient evaluations were supportive of implementation of each DA, however, the online DA3 was evaluated as having the least facilitators.

The format of the implemented DAs as well as their level of information density varied [24-26]. DA1 and DA2 could be incorporated in clinical consultation, or used at home, while DA3 was, by design, supposed to be used outside of consultations. Despite the variation between DAs, implementation results showed the same variation between hospitals with each DA, and successful implementation (>80%) was only achieved in a limited number of hospitals. Increasing the number of hospitals for implementation, as DA2 was implemented at 16 hospitals, compared to 8 and 9 hospitals for DA1 and DA3, did not result in more hospitals with successful implementation. This could suggest that for each DA support was present in some hospitals prior to the start of implementation, and that for upscaling implementation more structural encouragement and monitoring of implementation progress is needed in hospitals were the baseline support (in terms of care providers attitude or available resources) for DAs might be lower.

When patient-perceived barriers were reported, most were related to DA characteristics (unpractical, unadjusted to needs) or expectations (no confidence, expected no benefits or reduction of uncertainty). Although overall report of barriers was low, barriers were reported most often for the online, elaborate DA3, and least for the very concise hybrid DA2. However, both DAs achieved similar implementation rates that were lower than the concise paper DA (DA1). This finding seems inconsistent with previous studies concluding that web-based DAs are the most promising modality for improving implementation [28, 29]. However, care providers have also shown hesitance towards online tools [30, 31]. Future research is needed to gain a deeper understanding of how the benefits of online tools, such as tailoring to patient information needs and enabling interactive VCEs, can be balanced with patients' apparent preference for a more concise,

paper format. One solution might be to provide concise, paper add-ons to online tools, which can be introduced during consultation and may enhance the user friendliness of online tools.

The joint implementation efforts by the JIPPA consortium may have contributed to raising national awareness for SDM in both urology and oncology in the Netherlands. Many care providers have been introduced to the DA and to the principles of SDM, and during the course of the projects, consortium members contributed to national Pca treatment guidelines with a section on SDM and DAs (www.oncoline.nl). Therefore, the study in itself increased awareness for SDM and the existence of DAs and educated many teams in using DAs in clinical routine. However, it may also have caused a barrier, as clinical practice was unclear about which DA should be applied, and what the differences between the available DAs entailed. To the best of our knowledge, no earlier studies have reported (national) implementation rates for Pca DAs, and comparability to other DA implementations studies is difficult to interpret as they were aiming at different patient populations (e.g. women with breast cancer, or orthopedic patients) and settings (e,g, screening decisions often include the general practitioner) [10, 11, 32] Further research is needed to determine if having different types of DA can help implementation since patients and care providers can select the DA they prefer most, or that the variety in available DAs hinders implementation since each DA has its specific characteristics and usability aspects that require training. Moreover, future research could study if specific DA characteristics have an effect on implementation rates, by randomizing distribution of different DA types across hospitals.

A strength of the current study was that we were able to investigate implementation of three DAs by using a similar questionnaire at a similar point in time. As a consequence of studying three different DAs, sample size and number of participating hospitals was higher than most previous Pca DA studies [9, 33]. Eventually, one in three Dutch hospitals was exposed to one of the three DAs. Hospitals from different levels (academic and non-academic) and from different regions were included in the study, increasing the generalizability of our findings.

A limitation of the current study is that the implementation rate was calculated based on *actual* receivers of a DA as proportion of an *estimation* of the total number of eligible patients. Since the number of patients eligible for study inclusion were not systematically registered by each of the three DA studies, we relied on the hospital specific retrospective cohorts of PCa patients from the cancer registry. This ensured the sample was determined via the same method for every hospital. However, since the total number of patients eligible for DA receipt was estimated, this entailed that

no information was available about patient characteristics from those patients who were possibly eligible but were not offered a DA. In particular in hospitals with low implementation rates, a selection bias could have occurred if only patients were included who favored DA use. Another limitation is that the implementation period was not exactly simultaneous for all three DAs. Implementation of DA1 started almost a year ahead of DA2 and DA3. Moreover, a previous version of DA1 was studied in an earlier trial, which could have helped achieving the higher overall implementation of DA1 [26]. Furthermore, each participating hospital was linked to one of the three regions, and consequently implemented its respective DA. Possibly, some patients or care providers could have been more supportive of another DA and overall DA uptake would have been higher if all formats would be matched according to patient or care providers' preferences. For example, one patient might benefit more from an elaborate DA, while for another patient optimal understanding and satisfaction is reached with a concise DA [34-37]. Finally, no information was available from patients who received, and possibly also used a DA but did not consent to participate in the survey study.

Patient evaluations from the three DAs in the current study were all favorable towards implementation. To further understand the observed differences in implementation rates between hospitals, future steps towards sustained DA use should include further investigation into barriers at the level of care providers and organizational barriers.

Conclusion

Overall implementation rate of the DAs in clinical routine was 40%. A wide variation in uptake across hospitals was observed for each DA. Most patients were satisfied with the DA they received, and only few barriers of usage were perceived by patients. Offering an online-only DA led to less patient-reported facilitators compared to a paper-only or hybrid DA.

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Chapter 11

SUMMARY AND GENERAL DISCUSSION

SUMMARY OF RESULTS

In this chapter, the main findings of the studies reported in this thesis are summarized. Based on these results, considerations for DA development and implementation, and implications for clinical practice and future research are discussed.

This thesis started with an investigation into the preferences for involvement into treatment decision-making and satisfaction with information received in a sample of Pca patients who already chose a treatment previously (**Chapter 2**). For seven hospitals within the southern area of the Netherlands Cancer Registry (NCR), a random selection of 150 Pca patients per hospital was made consisting of patients diagnosed between 2006 and 2009. These patients were sent a questionnaire measuring decision-making role preferences and the evaluation of information received, within the Patient Reported Outcomes Following Initial Treatment and Long-Term Evaluation of Survivorship (PROFILES) Registry. After exclusion of high-risk Pca patients, who fall out of the scope of this dissertation, response was obtained from 562 patients with low- or intermediate risk Pca (response 71%). A majority of these men preferred a collaborative (shared patient-doctor) or active (patient-driven) decision-making role (81%), and 19% of the men in our sample preferred a passive (doctor-driven) role in treatment decision-making. A disadvantage of the measure that was used to determine role preferences (Control Preferences Scale) consisted of not being able to differentiate between a preference for involvement into the decision *process* or the for making the decision itself, which could be different. Men who preferred a passive role were significantly older and less educated compared to both other role preference groups. Information satisfaction was lower for men with a passive role preference, they reported to have received less information, and judged the information as less helpful. Across all role preferences groups, between 25-30% of men indicated they would have wanted to have received more information before they made their treatment decision. However, the cross-sectional design of this study did not allow to infer causality from these results.

Where chapter 2 retrospectively assessed satisfaction with information, and the relation with decision role preferences, we intended to obtain more insights in the impact of receiving a Pca diagnosis and the following process of treatment selection. Therefore, we undertook a prospective study including patients when scheduled for prostate biopsy because Pca was suspected, but had not been confirmed yet (**Chapter 3**). It is known that many patients experience a decline in health-related quality of life (HRQoL) as a consequence of Pca treatment and its associated side-effects. Our expectations were that a decline in HRQoL would already appear before treatment onset as a result of the burden of receiving the diagnosis and choosing a treatment. Moreover, we were

interested if individual differences (optimism, self-efficacy, and personality traits) were associated with changes in HRQoL before treatment onset. Patients with suspected Pca (*n*=377) were surveyed before biopsy, making this study one of the first to take a pre-diagnosis baseline measure. In case PCa was detected (*n*=126), a follow-up questionnaire was sent after treatment was chosen but had not yet started. Compared to the pre-diagnosis baseline, HRQoL was lower after receiving a Pca diagnosis and selecting treatment. In particular, role and cognitive functioning worsened, and elevated fatigue, constipation, and prostate specific symptoms were reported. In contradiction to the impaired overall HRQoL evaluation, sexual activity and functioning improved in the period between the first and second questionnaire. Baseline HRQoL was not associated to subsequent treatment choice, but if a curative treatment was chosen, worse HRQoL was reported at follow-up compared to men who chose active surveillance, however, it has to be noted that treatment subgroups at follow-up consisted of small samples, impairing statistical power of these findings. At baseline, an association between HRQoL and optimism was found, and at follow-up an association between HRQoL and self-efficacy. No associations with personality traits were found, indicating that no traits could be identified that predict how a patient would respond to being diagnosed with Pca (i.e. experience lower HRQoL after diagnosis).

Results from the studies presented in chapter 2 and chapter 3 supported the need for improved information provision and further support during Pca treatment decision-making. Decision aids (DAs) are interventions that have proven to be beneficial to help engaging patients and care providers in shared decision making (SDM). In absence of a Dutch DA with values clarification exercises for the treatment decision in Pca, a novel Dutch DA was developed (**Chapter 4**). A pre-existing, evidence-based, Canadian Pca DA, and consultation routines in Dutch clinical care were analyzed, in order to adjust the original DA to the Dutch context. Although patients were not directly involved to the development of current DA, all DA content was based on a cross-cultural study identifying which information is required by Pca patients when selecting treatment, including Dutch patients [1]. Usability testing (n=11) was undertaken with patients and care providers, and resulted in 212 comments, which were all addressed in final adjustments to the DA. Prior to enrollment of the DA in routine clinical care, patients and care providers consented that the DA was comprehensible and well-structured, and that use of the DA in routine care was recommended. Patients included in usability testing all recently made a treatment decision to ensure an accurate evaluation what is required when choosing treatment, without the distress resulting from just being diagnosed being present. Key features of the newly developed DA included presenting information about active surveillance separately from detailed information about curative treatments (surgery and radiotherapy), and values clarification exercises which

were designed as statements and required a tradeoff between treatment specific aspects (e.g. 'I fear surgery' (reason for radiotherapy) versus 'I do not fear surgery' (reason for surgery)).

To test the effectiveness of this newly developed DA, and to measure the level of implementation in clinical care, a cluster randomized controlled trial (RCT) was set up (**Chapter 5**). Within the Prostate Cancer Patient Centered Care (PCPCC) trial, eighteen Dutch hospitals were randomized to either include the DA during treatment counseling or to provide counseling as usual. Health care providers from the trial's intervention arm were invited to evaluate working with the DA, care providers in the control arm evaluated usual information routines. Patients who were newly diagnosed with Pca in one of the participating hospitals were invited to complete questionnaires after treatment was chosen (but before treatment started), and 6 and 12 months later. Log data from the DA and national cancer registry data were used to determine the level of implementation of the DA. The primary outcome measure of the PCPCC trial was patient reported decisional conflict, as it was hypothesized that including a DA during treatment counseling would lower decisional conflict. Secondary outcomes were patient satisfaction, preparation for decision-making, knowledge, and decisional regret. As previous studies found anxiety and depression symptoms to be common in Pca patients, in particular for patients who consider postponing immediate curative treatment by means of AS, we measured these symptoms (HADS) across all timepoints and included them in further analyses as covariate.

Patient-reported decision process parameters of the PCPCC trial, measured immediately after decision-making, were examined in **Chapter 6**. A total of 382 patients (DA arm, *n*=273; control arm, *n*=109) were enrolled in the trial, of which 336 participants (88%) filled out the first post-decision questionnaire. The levels of decision involvement and decisional conflict were comparable between patients from both trial arms. Patients with a DA felt more knowledgeable but scored equally well on a Pca knowledge test as patients from the control arm. Small, statistically significant negative effects were found on satisfaction with information and preparation for decision-making. A preference for a DA in print over online and depression and anxiety symptoms were negatively associated with satisfaction and conflict scores in the DA arm.

To assess regret, treatment satisfaction, and information satisfaction after Pca treatment was completed, participants in the PCPCC trial received follow-up questionnaires 6 months (n=336, response 92%) and 12 months (n=308, response 95%) after their initial treatment decision (**Chapter 7**). One year after treatment for Pca was chosen, most respondents reported very little regret about their decision and were satisfied with their

treatment and the information received. Main effects from the DA on these outcomes were not found. A less favorable patient-doctor relation and anxiety and depression symptoms were associated with increased odds of reporting regret about the chosen treatment.

In addition to positive patient evaluations, is commitment from care providers an important factor for sustained use of DAs in routine clinical practice. Previous studies showed that care providers' motivations are an important facilitator for implementation of DAs. In **Chapter 8** we assessed care providers' evaluation of DA usage in the DA arm of the PCPCC trial, and the evaluation of usual information routines among care providers from the control arm. From both trial arms, 108 care providers (urologists and nurses) were invited, and 63 filled out the questionnaire (response 58%). Care providers from the DA arm were supportive of the DA content and usability. Satisfaction with the DA was comparable to satisfaction with usual information among care providers from the control arm. However, care providers from the control arm did perceive that patients, with their usual information routines, already receive too much information. In contrast to earlier studies, care providers from both trial arms did not experience neither expect time barriers from DA use.

Next to assessing outcomes reported by patients and care providers, the PCPCC trial aimed to measure the level of DA implementation in routine clinical care (**Chapter 9**). The level of DA implementation within the PCPCC was determined per individual hospital by taking the number of DA users (based on DA log data) as proportion of the estimated total number of eligible Pca patients during the trial period, based on historical registry data. With 351 patients receiving a DA, the average achieved level of implementation was 35% across all hospitals. Between hospitals, implementation varied from 16% to 84%. After receiving the link to the online DA, most patients (79%) accessed the DA. In the post-decision questionnaire, 79% of the patients indicated that the DA summary was discussed with their doctor. With being one of the first studies to provide such detailed implementation and usage data, these results indicate that most patients used the DA once received, and that care provider and organizational (hospitals) factors should require further investigation in order to improve implementation.

The DA developed and tested within the PCPCC trial was one of three Dutch Pca treatment DAs that were simultaneously implemented in routine clinical care for newly diagnosed Pca patients in The Netherlands, within a collaboration of the Joint Implementation Prostate cancer Patient-centered care (JIPPA) consortium. These DAs varied in format, consisting of a 'concise paper DA' (i.e print booklet) , a 'very concise paper or online DA' (i.e presented in a diagram style with short explanations), and the

elaborate online-only DA as described in this dissertation. In the final empirical chapter of this dissertation (**Chapter 10**), we reported the joint JIPPA assessment of patient evaluations and implementation results across the three DAs. Although the regions in which each of the three DAs was evaluated were not randomly allocated, and patient groups differed, each DA achieved comparable patient evaluations and implementation rates across hospitals. Implementation across participating hospitals ranged from low (<20%) to (almost) complete implementation (80-100%) in all three trials. All DAs were well received by patients. With the 'concise paper only DA' and the 'very concise paper or online DA', most patients (96-99%) were satisfied with the DA format. For our online only DA, 21% indicated to have preferred a paper format instead. All DAs were handed out most often by the urologist (71-78% of the cases), and most patients (79-82%) perceived the urologist was also the most suitable person to hand out the DA. However, the majority of patients who received a DA from a nurse, perceived the nurse as most suitable care provider to hand out the DA (60%). When the DA was received within the first week after diagnosis, the largest proportion of patients (93%) felt this was the best moment.

GENERAL DISCUSSION

The research presented in this dissertation included (1) development, (2) implementation, and (3) evaluation of a web-based DA for patients newly diagnosed with early-stage Pca in everyday care in multiple healthcare centers in the Netherlands. This included the description of an alternative development method of adapting a pre-existing, evidence-based DA to a different language and cultural setting. In contrast to conclusions from the latest Cochrane review [2], commonly found DA effects (e.g. less decisional conflict, more knowledge) were not replicated in the PCPCC trial. At a 12-months follow-up, also no beneficial patient-reported outcomes were found. Evaluation of the DA implementation included structured reporting on uptake and usage, and allowed linkage of DA usage to the patient-reported outcomes. This revealed that patients with anxiety and depression symptoms or a preference for an offline DA, were less supportive of the current DA version. Finally, our consortium approach allowed to evaluate implementation results for three different Pca DAs in Dutch routine Pca care, showing that for each DA alike, implementation rates between hospitals varied widely.

Building on the results of the studies included in this dissertation, as summarized above, three themes require further discussion in this section. First, considerations about DA development will be discussed. Second, the most important methodological considerations (strengths and weaknesses) of the PCPCC trial will be reviewed here,

beyond specific strengths and limitations that have been discussed in previous chapters. Third, considerations about DA implementation will be discussed. This general discussion ends with implications for clinical practice and for future research, before a general conclusion is presented.

Considerations about DA development

The decision to develop an online-only DA was based on the high degree of internet access among the entire Dutch population (>97%) [3], and the wider possibilities to tailor information provision and present values clarification methods. We modified a pre-existing, evidence-based tool that was developed in Canada [4].Patients differ in their information needs, capabilities to process information, and their desired level of involvement into a medical (treatment) decision [5-7]. Yet, DAs aimed to support patient decision-making and initiation of SDM, have been developed according to a single one-size-fits-all format. Also the DA evaluated in this dissertation was developed to be universally applicable to all Pca patients. Perhaps it was for this reason that we learnt that 20% of participating patients would have preferred a paper format over the online format. This evaluation was actually provided by patients who consented to complete the questionnaires which were also online by default (paper on request). It could therefore be possible that these 20% of participants are actually an underrepresentation of the total population of Pca patients who would prefer to use a paper DA over an online DA. Although it was determined prior to DA development that almost all citizens in the Netherlands have internet access at home, it is possible that for a serious – potentially life threatening – disease, and the associated process of selecting treatment, many patients prefer an offline environment for information and decision support. Compared to online tools, which are often intended to be used outside consultations, an important advantage of offline tools is that they can be incorporated more easily in clinical consultations. Based on the results of the studies in this thesis, it can be suggested that patients who are lower educated and report anxious or depressive symptoms, could benefit from more counseling or integration of the DA into the actual clinical consultation. More variation in DA format and delivery methods in order to personalize to patients needs is therefore important. As seen within the JIPPA study, with the offline and more concise DAs, an even larger proportion of patients was satisfied with the format (chapter 10).

Compared to the other two JIPPA DAs evaluated in chapter 10, the current DA was the most extensive, and also the only to include explicit values clarification exercises (VCEs) (chapter 3). Such exercises help patients in the process of clarifying personal values that are relevant to the decision, and are therefore a widely recommended element in DAs [1, 4,

[8]. However, a clear definition of VCEs is not available, resulting in a broad variety of tasks that can be seen as values clarification, with most common exercises at least including the rating, ranking or discussion of pros and cons [8]. When patients engage in such exercises, this helps the cognitive processing of all options, offers time to process new information and to retrieve memories relevant to the decision. Furthermore, it allows comparing options and stimulates reviewing treatment-specific aspects or personal values that might not have been considered otherwise [9].

Inclusion of VCEs can be seen as an effort to stimulate deliberation about the presented treatment aspects. Whereas in many real-life situations, and for medical decisions specifically, the general assumption often is that deliberative analysis is the best strategy to make a decision, this may not always be the case [10, 11]. Earlier scenario-based studies suggested that this may result in people choosing treatment that has more risks than the disease itself or avoiding treatment with possible adverse effects, while the mortality risk of the disease is higher [12, 13]. Stimulating deliberation might result in people feeling better about their decision, as they put more effort in reaching a decision, while the decision itself might be the same and possibly still not provide an optimal patient-treatment fit [14 15]. This could have been reflected in the knowledge scores reported in chapter 6; while DA users felt more knowledgeable, their knowledge test scores were similar to the scores of participants from the control arm.

The VCEs within the current DA presented two unique treatment option attributes as a trade-off to elicit a preference towards one of the two presented treatments (e.g. the fear of postponing active treatment with AS versus undergoing possibly unnecessary active treatment with the risk for adverse effects; chapter 4). Although trade-offs have been recommended to reach value-congruent decisions [16], the tasks were developed without specific (evidence-based) development guidelines [16, 17]. The following two suggestions for further refinement and improvement of the DA in later DA versions may be considered. First, the VCE trade-offs in the current DA were presented with their corresponding treatment, however, identifying the associated treatment can influence preferences [18]. For a patient, the tendency to be consistent with a pre-existing (biased) preference could then be confused with the true treatment preference. Second, one in three DA users preferred a treatment advice as outcome after DA use, possibly caused by the expectation of receiving an output after providing input by answering the VCEs. Providing an advice would also have to include weighing of attributes, since one particular treatment aspect (e.g. avoiding adverse treatment effects) could outweigh all other presented treatment aspects. Including best-worse scaling of the current trade-offs could be considered [19].

Another development issue was the information density of the current version of the DA (chapter 4). According to Fuzzy trace theory, the delivery of this amount and type of precise information could be suboptimal to support decision-making. Fuzzy trace theory explains that people might rely on the gist of information, rather than its exact details.[20]. For future versions of the current DA, or for novel DAs, the amount of presented information should be reconsidered. Ongoing research in presentation of risk information provides opportunities to further optimize presentation of quantitative information, so that the risk for judgement biases and errors is minimalized, consisting of clear reference categories, the use of numbers over words, and additional visual formats, whereas in the current DA still large amounts of text were included [21-24].

Also, further developments in the dissemination of big data in healthcare, within the wider perspective of delivering value-based healthcare, could influence the future approach to DA development [25, 26]. Evaluating appropriate and effective care is increasingly relying on big data analyses. Insights that become available in this way, may also be useful for other purposes in the care process, such as decision support. For example, presenting the best available scientific evidence in a DA, can include presenting a broad margin of uncertainty (e.g. 'between 40 and 80 out 100 patients will experience side effect X'). For a local hospital, individual doctors, and individual patients, other, more accurate, risk estimates may apply, and become insightful from big data analysis. In recent years, the number of studies into practical applications of big data to use in individual decisions has increased dramatically, and can enable personalized estimates of the effectiveness of different treatments [26]. Within Pca care, personalized risk estimates can already be calculated for Pca screening or suitability of patients for active surveillance, based on individual patient characteristics, [27-31]. Cancer in general, and cancer treatment choices specifically, are fields where data does not only come from scientific studies, but many (national) cancer registries routinely collect relevant data as well. With current developments in these fields, big data could be integrated into DAs and VCEs to present data in a personalized format, with risk estimation, and outcome predictions relevant to the individual patient. However, most of the data that are available for such analyses were not collected with the intention to support decision-making. It should therefore be critically evaluated it the available data is relevant to the individual patient.

Methodological considerations PCPCC trial

A main strength of the Prostate Cancer Patient Centered Care (PCPCC) trial (Chapters 5-10) entails the cluster randomized design. With cluster randomization, hospitals were randomized to the DA arm or control arm, instead of randomizing individual patients. As a result, all patients within the same hospital received the same care, and

care providers did not need to switch between DA counseling and usual counseling per patient. This avoided the risk of contamination of the usual care arm with components of DA counseling.

Another important advantage of cluster randomization was that the DA intervention could be included in clinical routine as naturally as possible, without having an artificial randomization procedure before handing out a DA or not. This is why a cluster randomized design is recommended when the studied intervention includes changes in clinical routine and care providers' behavior [32]. Moreover, patients in our trial were not aware of randomization, and thus the existence of two separate trial arms. Patients from both trial arms were informed about a questionnaire evaluating the process of information provision and treatment decision-making, without explicitly mentioning that the DA was part of the study.

Furthermore, participants in the control arm were not aware that a novel tool was not available to them. Participants being blinded to trial arm reduces the risk for potential biases, as participants are less likely to behave differently, or to provide answers they expect are desirable for the study [32]. Care providers and researchers within the PCPCC trial were aware of randomization and assignment of hospitals to their respective trial arm. This aspect is discussed further on as a potential limitation.

A second strength is the pragmatic approach that was chosen during the PCPCC trial. During the introduction to the trial, care providers were advised to distribute the DA immediately after diagnosis, or at the moment other information materials were provided, in case this was at a later moment. However, to let the DA fit as natural as possible with existing routines during clinical consultations, hospitals and care providers were free to select the exact moment they felt was optimal to hand out the DA to the patient. In this way, enrolling the DA into clinical routine was as least disruptive for existing work flows as possible. Consequently, the effectiveness of the DA intervention could be measured including real-life practice conditions [33]. As many previous DAs failed to achieve structural implementation in routine clinical practice after their initial clinical trial, the pragmatic approach of the PCPCC was essential to gather evidence of uptake of the DA under real-life conditions [34, 35].

However, this methodology also resulted in important limitations. One limitation was the unbalanced recruitment of participants in both trial arms. The required sample size for the PCPCC trial was estimated at 225 participants per trial arm (aiming at 25 patients per hospital). Although conservative sample size calculations were made, inclusion in the control arm stagnated at n=109. Moreover, none of the nine hospitals

in the control arm completed recruitment of the required number of 25 participants. During the same period of time, an equal amount of hospitals in the intervention arm did succeed in completing the required sample. Therefore, it is very likely that selection bias was introduced into the control arm with care providers being more selective in which patients they recruited to enroll in the trial, while care providers in the DA arm could have been more motivated to include patients as they were supportive of DA use [36]. Although comparison between available patient characteristics did not indicate substantial differences between samples from both trial arms, it remains possible that patients who were more likely to consent in the control arm had different characteristics compared to participants from the intervention arm. Post-hoc analyses revealed that with the current sample statistical power was still sufficient (>.8) to detect medium effects (*d*=.04), but low for smaller effects. Also, with five hospitals in the control arm including less than 10 participants, meaningful hospital specific effects could not be determined within this trial.

A second limitation, as mentioned earlier, is related to the awareness among care providers of trial assignment and aim of the study. Care providers in the DA arm were aware that the DA was tested within their hospital, and care providers from the control arm knew results from the DA arm would be compared to the results from their usual care. Emphasis on the novelty of the DA could have led to a more critical evaluation by participants in this arm, while care providers in the control arm could have been more motivated to engage in SDM as they were aware of comparison with the DA arm (performance bias) [37, 38]. Moreover, the unbalanced sampling between both arms (2:1 ratio) suggests fewer eligible patients were enrolled in the control arm as compared to the intervention arm. This could have introduced sampling bias in the control arm, with patients who were likely to be (very) satisfied with usual care, being included more often compared to patients who appeared to be more critical or distressed following diagnosis. However, the JIPPA DA evaluations in chapter 10 showed similar findings, while these evaluations were obtained from trials that had different designs and methods of patient inclusion.

A third limitation was that implementation of the DA was linked to participation in the PCPCC trial. With our pragmatic approach we tried to enroll the DA as natural as possible in clinical routine. However, with each DA that was handed out during the trial period, the questionnaire study within PCPCC trial needed to be explained to patients as well. Although patient consent was not needed to use the DA, and patients were free to use the DA without consenting to participate in the trial, explanation about the trial and informed consent forms were introduced at each moment the DA was also introduced. Having to explain the trial could have been a barrier for care providers, while patients

who refused to participation in the PCPCC trial might have been unaware that the DA could still be used and was part of the 'new' usual care. Because treatment preferences from both the care provider and patient were collected before DA usage, it was not possible in this study to ask for consent at a later point after the DA was introduced.

Considerations about DA implementation

The hybrid efficacy-implementation design of the PCPCC trial, enabled to test the tool in its natural environment, while simultaneously collecting data on implementation (chapters 5-9). The evaluation of DA implementation included registry data about the estimated total number of eligible patients, and DA log data provided insights in actual DA usage. Many previous studies were not able to report these parameters due to their study design or DA format (e.g. paper). Furthermore, a 12-months follow-up, as presented in chapter 7, is rare in DA research. Finally, the JIPPA consortium approach to joint DA implementation and evaluation was promising; most patients used the DA that was received, and all DAs were evaluated positively. With the three DAs, the JIPPA consortium engaged 33 Dutch hospitals in DA use and SDM, which would not have been achieved with an individual trial.

A main implementation result from the PCPCC trial was the wide variation in DA uptake across participating hospitals (Chapter 9). Similar patterns of implementation were obtained by the two other Pca DA initiatives that were enrolled simultaneously in other hospitals across The Netherlands (Chapter 10).

The current DA was implemented with a minimum of requirements or usage guidelines. Possibly, more training is needed on how to introduce the DA and integrate discussion of the DA summary into treatment counseling. Earlier studies showed that care providers can overestimate the extent of SDM they are already applying, and misinterpret patient preferences for involvement [39-41]. Following these mechanisms, some care providers in the PCPCC trial possibly underestimated patients' eligibility for a DA, in terms of willingness and capability, and the need to introduce the DA to patients. Structural feedback on DA distribution across hospitals and between individual care providers, and structural patient evaluations could provide insights into how many patients were reached compared to relevant peer groups (other doctors and/or other hospitals), and where improvements in distribution routines are possible based on patient evaluations.

A second consideration on DA implementation following the PCPCC trial is the total information load for patients after Pca diagnosis. In the current trial, the DA was added to all existing information routines. Usually patients receive oral information from their care provider(s), and hospital specific materials about their disease, treatments,

and procedures. Often, additional information is provided from national organizations (e.g. Dutch Cancer Society, patient association), and are patients referred to additional websites (e.g. Dutch urology association). Besides the information that is received at the hospital, various other sources are available to the patient as well (e.g. general practitioner, health insurer, own searches for (online) information, and personal networks). In this overwhelming availability of information of varying quality, it can be challenging for patients to determine which source is the most reliable or helpful [42]. Instead of piling new information sources on existing materials, it should be considered to introduce the DA as primary information and decision tool, and adjust or incorporate existing (hospital) information materials into the DA.

Implications for clinical practice and future directions

The PCPCC trial did not replicate effects that are typically found in DA studies (i.e. lower decisional conflict, higher information satisfaction, more knowledge) [2]. Partly this was due to unexpected positive outcomes in our control arm (chapter 6). As discussed in previous sections, this could have been caused by care provider effects or selection bias. However, it could also be that current routine Pca care in The Netherlands already involves patients better into the decision process and informs them better compared to what we reported in the retrospective cohort of Pca survivors (chapter 2) or control groups included in previous international studies [2]. Moreover, SDM has emerged in the past decade in The Netherlands, not only by endorsement from researchers and clinicians, but implementation of SDM is also encouraged by government, health insurers, and patients associations [43]. Therefore, with the wide body of evidence available on the beneficial effects of DAs, and still increasing awareness for SDM, make it likely that DAs in some format will continue to be included in clinical practice [2, 43].

In this context, an important continuation of the studies presented in this thesis relate to the role of DAs in the broader context of SDM. Many other studies have looked into the effects of DAs on patient-reported outcomes (e.g. decisional conflict, and perceived SDM) and decision outcomes (e.g. selected treatment) for other diseases and screening decisions; the latest Cochrane review (2017) included 105 studies[2]. And apart from these DA studies, much more literature is available that describes the model, and benefits of SDM itself [44-47]. As also explained in this dissertation, it is often assumed that DAs help to initiate SDM, and that the beneficial effects after DA use are the result of more SDM occurring. Consequently, it is often advised that more DAs are needed in order initiate and facilitate SDM. It can however be questioned if beneficial effects from DAs are the result of (more) SDM occurring, or solely effects from the DA itself (e.g. more knowledge, increased self-efficacy) [48]. The studies included in this dissertation did not

directly measure the impact from the DA on SDM. Although both patients and care providers evaluated the current DA positively in their respective evaluations (chapter 6 and chapter 8), we did not measure the degree of SDM occurring before or after the DA intervention. Moreover, we had no direct observations of how consultations looked like when the DA was introduced, or when the DA summary was discussed. That DAs and SDM are beneficial to patients and overall quality of care, is well supported by scientific literature, however, DAs are not SDM and vice versa, more studies are needed that investigate the role DAs have in SDM outcomes [2, 24, 48, 49] .

General conclusion

Treatment decisions in Pca care are preference-sensitive and require careful consideration by patients and care providers to select the best suiting treatment. To support patients, and guide both patients and care providers during the treatment decision-making process, a Dutch web-based DA was developed to help patients construct an informed treatment preference. The DA was positively evaluated by patients and care providers. However, no substantial effects from the DA on patient-reported outcomes were detected within our PCPCC trial. The pragmatic approach of our trial allowed to investigate the DA in the context of routine clinical care, but also introduced a risk for selection and performance bias into the study. DA effects could be more subtle when the DA is part of routine care instead of what has been found in more controlled clinical trials. Methodological limitations prevented a meaningful investigation of hospital specific effects or specific patient subgroups, and should be addressed in future studies. However, following the results, the most important implications for clinical practice relate to DA development and implementation. Future DA developments and adjustments to the current DA should consider their format and the construction of VCEs, and incorporate the possibility to tailor according to specific patient needs (e.g. anxiety and depression). Achieving high implementation rates in many hospitals proved to be difficult, and this finding was confirmed in parallel implementation studies from two other Pca DAs within the JIPPA consortium.

From an ethical perspective, patients should be offered all available resources -including DAs- in order to be fully informed about all treatment options. Clinical guidelines, patient and professional associations, and health insurers should therefore advice that all preference-sensitive (treatment) decisions should include a DA. This ensures individual treatment decision-making processes are less dependent on the performance and engagement of individual care providers. Moreover, it helps patients and care providers

to structure the process of informing and deciding about treatment. To upscale DA implementation, care providers should receive more training in distribution routines and including DA components into clinical counseling as part of SDM.

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Appendices

NEDERLANDSE SAMENVATTING

De studies in dit proefschrift hebben allen betrekking op de behandelkeuze bij gelokaliseerd prostaatkanker.

In **hoofdstuk 2** werd onderzocht welke voorkeur voor betrokkenheid bij de behandelkeuze patiënten hadden die reeds eerder een behandeling voor prostaatkanker kozen. Daarbij werd tevens onderzocht of er een verband was tussen die voorkeur en hun tevredenheid over de informatie die ten tijde van de behandelkeuze was ontvangen. Hierover vulde 562 respondenten, bij wie tussen 2006 en 2009 prostaatkanker werd vastgesteld, een vragenlijst in. Een meerderheid van de respondenten had op het moment van invullen van de vragenlijst een voorkeur om bij een behandelkeuze samen met de arts of (voornamelijk) zelfstandig te beslissen (81%). Negentien procent van de respondenten gaf de voorkeur aan een passieve rol, waarbij voornamelijk de arts het initiatief heeft. De groep respondenten die een voorkeur voor deze passieve rol uitsprak was ouder en lager opgeleid in vergelijking met de respondenten die een voorkeur hadden voor een gezamenlijke of actieve rol bij de besluitvorming. Respondenten met een voorkeur voor een passieve rol bleken vaker een niet-invasieve behandeling (afwachten of bestraling) te hebben ondergaan in vergelijking met de andere groepen. Ook was deze groep minder tevreden met de informatie die ten tijde van de behandelkeuze was ontvangen, gaf het aan minder informatie te hebben ontvangen, en vonden de ontvangen informatie minder nuttig dan respondenten met een andere voorkeur. Ongeacht de uitgesproken voorkeur voor een bepaalde beslisrol, had 25-30% van de respondenten liever meer informatie ontvangen ten tijde van de behandelkeuze.

Om vervolgens dieper in te gaan op de impact die het ontvangen van de diagnose prostaatkanker en het daarop volgende proces van behandelkeuze hebben, wordt in **hoofdstuk 3** een prospectieve studie beschreven die patiënten volgde vanaf het moment dat prostaatkanker vermoed werd, maar nog niet was vastgesteld. Hiervoor werden patiënten die een afspraak hadden om een prostaatbiopt te laten nemen gevraagd om deel te namen aan een vragenlijstonderzoek. Een belangrijke uitkomstmaat in dit onderzoek was gezondheidsgerelateerde kwaliteit van leven (KvL). Reeds bekend was dat de behandeling van prostaatkanker -meer nog dan ziekte zelf- kan leiden tot een daling van KvL bij patiënten, die zich pas in de loop der jaren weer hersteld. Vanwege de impact van de diagnose en de belasting van het kiezen van een behandeling was echter het vermoeden dat een daling in KvL al merkbaar zou zijn vanaf het moment van diagnose en niet pas bij de start van behandeling. Daarnaast werd onderzocht of er

een verband bestond tussen veranderingen in KvL en persoonskenmerken die relevant zouden kunnen zijn bij diagnose en behandelkeuze (o.a. optimisme, self-efficacy en persoonlijkheid).

Voorafgaand aan biopsie vulden 377 deelnemers de vragenlijst in. Bij 126 van hen werd er prostaatkanker vastgesteld en zij ontvingen een tweede vragenlijst nadat een behandeling was gekozen maar nog niet was gestart. Op het tweede meetmoment rapporteerde deelnemers een lagere KvL dan bij de eerste meting. Ondanks dat er bij deze patiëntengroep tussen de twee metingen weinig medische veranderingen te verwachten waren, werd er slechter cognitief en rol (werk en prive) functioneren gerapporteerd en meer vermoeidheid, constipatie en prostaat-specifieke klachten in vergelijking met de eerste meting. In tegenstelling tot de slechtere algemene KvL, werd er wel een verbeterde seksuele activiteit en functioneren gerapporteerd. In het geval dat prostaatkanker werd vastgesteld, waren de KvL scores die werden gemeten bij het biopt niet voorspellend voor een latere behandelkeuze. Echter, bij de tweede KvL meting bleek een lagere KvL vooral gerapporteerd te worden door respondenten die kozen voor een actieve behandeling (operatie of bestraling), en werd er minder verschil gevonden bij patiënten die kozen voor een actief volgen beleid. Bij de eerste KvL-meting, voorafgaand aan diagnose, werd er een associatie gevonden met optimime. Bij de tweede meting werd een samenhang met self-efficacy gevonden. Er werd geen verband gevonden tussen verandering in KvL en persoonlijkheid.

De voorgaande twee hoofdstukken belichtte verschillende aspecten (beslisrol, tevredenheid met informatie, KvL bij diagnose en behandelkeuze) uit het proces van diagnose en behandelkeuze bij prostaatkanker. Uit deze en eerdere onderzoeken, en ervaringen uit de praktijk, is bekend dat samen beslissen tussen arts en patiënt bij een behandeling voor prostaatkanker moeilijk is. Naast alle medisch relevante informatie, moeten de arts en patiënt ook overleggen over de persoonlijke situatie en voorkeuren van de patiënt. Een keuzehulp is in zo'n situatie een nuttig hulpmiddel voor arts en patiënt om tot een gezamenlijk behandelbesluit te komen. Een keuzehulp bevat vaak taakjes of opdrachten die patiënten helpen om hun eigen waarden en voorkeuren te verhelderen. In Nederland was nog geen geschikte keuzehulp voor prostaatkanker beschikbaar met dergelijke waarde verhelderende oefeningen. De ontwikkeling van deze keuzehulp wordt in **hoofdstuk 4** beschreven.

De keuzehulp is gebaseerd op een Canadese versie waarnaar eerder onderzoek is gedaan. Na observaties bij Nederlandse consulten, werd de keuzehulp aangepast aan de Nederlandse praktijk. De medisch inhoudelijke informatie werd geverifieerd aan de geldende Nederlandse en Europese behandelrichtlijnen. Met de nieuw ontwikkelde

conceptversie van de keuzehulp werd vervolgens gebruikersonderzoek gedaan met 11 deelnemers. Deelnemers waren zowel patiënten als zorgverleners (urologen, verpleegkundigen en een radiotherapeut). Er werd gekozen voor patiënten die reeds een behandelkeuze voor prostaatkanker hadden gemaakt omdat verwacht werd dat zij beter in staat zouden zijn om te reflecteren op wat noodzakelijk en nuttig is om aan te bieden in een keuzehulp voor prostaatkanker. Nieuw gediagnosticeerde patiënten zijn vaak nog belast met de emotie van de diagnose, en voor willekeurige testpersonen is het vaak moeilijk om zich in te leven in een situatie waarbij men voor de behandelkeuze bij prostaatkanker staat.

De deelnemers aan het gebruikersonderzoek gaven 212 opmerkingen over het gebruiksgemak, inhoud en indeling van de keuzehulp. Alle opmerkingen werden geanalyseerd en verwerkt in aanpassingen aan de keuzehulp. Voordat de keuzehulp werd geïntroduceerd in de praktijk, waren alle deelnemers aan het gebruikersonderzoek het eens dat de keuzehulp duidelijk en goed gestructureerd was, en dat gebruik in de dagelijkse praktijk aan te bevelen was.

Een belangrijk element uit de keuzehulp bestaat uit het opdelen van informatie over behandelen in twee delen, waardoor patiënten niet overladen worden met alle informatie ineens. In het eerste deel wordt uitleg gegeven over actief volgen in vergelijking met behandelen in het algemeen, daarna volgt pas gedetailleerde informatie over operatie en bestralen. Een tweede belangrijk element uit de keuzehulp zijn de waarde verhelderende oefeningen. Deze oefeningen bestaan uit stellingen waarbij telkens een afweging gemaakt moet worden tussen aspecten van een behandeling (bijv. 'Ik ben niet angstig voor een operatie' versus 'Ik heb angst voor een operatie'). Voorkeur voor de eerste stelling zou een reden kunnen zijn om voor operatie te kiezen, terwijl een voorkeur voor de tweede stelling een reden kan zijn om voor bestraling te kiezen. Op een samenvatting, die door de keuzehulp wordt gegenereerd worden de voorkeuren op alle stellingen weergegeven en kan de patiënt samen met zijn arts bespreken welke aspecten hij het meest belangrijk vindt en waar hij nog vragen over heeft.

Om het effect van deze keuzehulp en de implementatie in de dagelijkse praktijk te onderzoeken is een cluster gerandomiseerde studie opgezet. De studieopzet wordt beschreven in **hoofdstuk 5**. Binnen deze *Prostate Cancer Patient Centered Care (PCPCC) trial* werden achttien Nederlandse ziekenhuizen gerandomiseerd naar de interventie of controle arm van de studie. In de interventie-arm werd de keuzehulp toegevoegd aan het bestaande prostaatkanker-zorgpad. Hierdoor ontvingen patiënten na de diagnose en bovenop alle andere informatie, ook een uitnodiging om de keuzehulp te gebruiken. In de controle arm werd de standaard zorgverlening voortgezet zoals gebruikelijk was.

De studie kende een pragmatisch karakter waardoor per ziekenhuis de keuzehulp zo goed mogelijk kon worden aangesloten op gebruikelijke werkwijzen. Hierdoor was het mogelijk om invloeden uit de dagelijkse praktijk die effect konden hebben op de uitkomst mee te nemen in het onderzoek.

Na inclusie werd aan deelnemende patiënten op drie momenten een vragenlijst voorgelegd; na de behandelkeuze (maar voor de start van behandeling), en 6 en 12 maanden later. In de interventie-arm werd aan de hand van gebruikersdata uit de keuzehulp vastgelegd in welke mate keuzehulp daadwerkelijk werd gebruikt. Aan de hand van historische patiëntaantallen (uit de kankerregistratie) werd per ziekenhuis bepaald hoeveel procent van het aantal nieuwe prostaatkankerpatiënten werd bereikt met de keuzehulp. De primaire uitkomstmaat van de studie was de mate van gerapporteerde keuzeconflict over de gemaakte behandelkeuze. De hypothese was dat met behulp van een keuzehulp, patiënten minder keuzeconflict zouden ervaren. Secondaire uitkomsten bestonden uit tevredenheid met ontvangen informatie, voorbereiding op besluitvorming, prostaatkanker-specifieke kennis en spijt van de behandelkeuze. Aanvullend aan het onderzoek onder patiënten, werd aan zorgverleners een vragenlijst voorgelegd om de gebruikelijke informatievoorziening (controle arm) en werken met de keuzehulp (interventie arm) te evalueren.

De resultaten die betrekking hadden op het keuzeproces, inclusief het effect van de keuzehulp op keuzeconflict, is beschreven in **hoofdstuk 6**. Er waren 382 deelnemers in de PCPCC studie (273 in de keuzehulp-arm en 109 in de controle arm), waarvan uiteindelijk 336 respondenten de eerste vragenlijst hebben ingevuld (respons 88%). In tegenstelling tot de hypothese bleek de mate van keuzeconflict vergelijkbaar tussen respondenten uit beide groepen. Ook werden er geen verschillen gevonden in de mate van betrokkenheid bij het keuzeproces. Respondenten uit de keuzehulp-arm vermoedde meer kennis te bezitten dan respondenten uit de controle arm, maar respondenten uit beide groepen behaalden vergelijkbare scores op een kennistest. Ten opzichte van de controle arm, werden in de keuzehulp-arm kleine, maar statistisch significante, negatieve effecten gevonden op tevredenheid met informatievoorziening en voorbereiding op de besluitvorming. Angst en depressie symptomen en de voorkeur voor een keuzehulp op papier in plaats van online waren geassocieerd met lagere tevredenheid en conflict scores in de keuzehulp-arm.

Om te onderzoeken of het beslissen met of zonder keuzehulp effecten had op spijt, en tevredenheid met de behandeling en informatie op langere termijn, werden deelnemende patiënten binnen de PCPCC-studie gevolgd voor 12 maanden (**hoofdstuk 7**). Zes (n=336, respons 92%) en twaalf maanden (n=308, respons 95%) nadat de

behandelkeuze werd gemaakt ontvingen alle deelnemers vervolgvragenlijsten. Uit de resultaten bleek dat de meeste patiënten een jaar na de behandelkeuze weinig spijt hadden van hun keuze en tevreden waren met de informatie die destijds was ontvangen. Hierbij werden geen verschillen gevonden tussen de keuzehulp en controle arm van de studie. Een minder positieve patiënt-dokter relatie en angst en depressie symptomen bleken verband te houden met het rapporteren van spijt over de behandelkeuze.

Naast een positieve patiëntevaluatie is commitment van zorgverleners een belangrijke factor voor duurzame implementatie van keuzehulpen in de dagelijkse praktijk. In **hoofdstuk 8** werd de keuzehulp door zorgverleners uit de PCPCC -studie geëvalueerd. Aan zorgverleners uit de controle arm werd om een evaluatie van de gebruikelijke informatievoorziening gevraagd. In totaal werden 108 zorgverleners (urologen en verpleegkundigen) uitgenodigd voor een vragenlijst-onderzoek (respons 58%, n=63). Uit de resultaten bleek dat zorgverleners uit de keuzehulp arm tevreden waren over de inhoud en gebruiksgemak van de keuzehulp. Tevredenheid met de keuzehulp was vergelijkbaar met de tevredenheid over de gebruikelijke informatievoorziening door zorgverleners uit de controle arm. Zorgverleners in de controle arm waren van mening dat met de gebruikelijke informatie, patiënten al het risico lopen om te veel informatie te ontvangen. In tegenstelling tot eerdere studies, werd er geen tijdsdruk ervaren door zorgverleners als gevolg van het werken met de keuzehulp, en werd dit ook niet verwacht door zorgverleners in de controlegroep.

In de PCPCC studie werd naast de evaluatie door patiënten en zorgverleners ook de implementatie in de dagelijkse praktijk onderzocht (**hoofdstuk 9**). Precieze inschattingen van de implementatiegraad en mate van daadwerkelijk gebruik van de keuzehulp zijn vaak moeilijk te bepalen. Doordat de huidige keuzehulp web-based is, gebruikers een persoonlijke inlogcode ontvingen, en er informatie beschikbaar was over de vermoedelijke omvang van de totale patiëntengroep, konden zowel implementatie als gebruik nauwkeurig in kaart gebracht worden. Binnen de studieperiode verschenen ongeveer 1.000 prostaatkankerpatiënten in de deelnemende ziekenhuizen, waarvan er 351 de keuzehulp hebben ontvangen (implementatiegraad 35%). Tussen ziekenhuizen varieerde de implementatie tussen 16 en 84%. Na ontvangst, logde de meeste patiënten in de keuzehulp in, en in de vragenlijst gaf 79% van de patiënten aan dat de samenvatting uit de keuzehulp was besproken met de uroloog.

Gelijktijdig met de PCPCC vonden twee andere studies naar keuzehulpen voor prostaatkankerpatiënten plaats in Nederland, onder de naam JIPPA (*Joint Implementation Patient-centered care*). De drie onderzochte keuzehulpen verschilden van elkaar in format (papier of online), hoeveelheid informatie (beknopt tot uitgebreid) en waarde

verhelderende opdrachten (wel of niet). De evaluaties van de keuzehulpen door patiënten werd volgens dezelfde methode uitgevoerd. Hierdoor konden de resultaten van de patiëntenevaluaties uit de drie verschillende onderzoeken met elkaar vergeleken worden (**hoofdstuk 10**). In iedere studie werd de keuzehulp positief beoordeeld door patiënten en werden vergelijkbare implementatieresultaten gevonden. Met een beknopte keuzehulp op papier waren de meeste patiënten tevreden. Bij de uitgebreide online keuzehulp had een deel van de patiënten liever een keuzehulp op papier ontvangen. De meeste patiënten ontvingen de keuzehulp van de uroloog, en beoordeelde de uroloog ook als meest geschikte persoon om de keuzehulp uit te reiken. Echter, van de patiënten die de keuzehulp van een verpleegkundige ontving, vond 60% de verpleegkundige het meest geschikt. De eerste week na diagnose werd door de meeste patiënten als het beste moment aangegeven om de keuzehulp te ontvangen.

DANKWOORD

Een proefschrift is geen proefschrift zonder een overdreven lang dankwoord. Paradoxaal genoeg ben ik mij ervan bewust dat ik de minste tijd besteed aan het schrijven van dit stuk, terwijl het waarschijnlijk het best gelezen hoofdstuk is. Al weten de mensen die mij goed kennen dat dat misschien ook niet helemaal waar is. Van die tijd dan.

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tweede auteur van bijna alle hoofdstukken, schrijf je een eigen proefschrift en doe je tussendoor ook nog even de opleiding tot uroloog. Je draait je hand er niet voor om, en daarom weet ik ook zeker dat ik mij geen betere paranimf kan wensen.

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Op de universiteit in Tilburg liep ik met mijn medische onderzoek rond op een afdeling met voornamelijk sociaal psychologen. Dat is een wereld die vooral bestaat uit veel experimenten in een lab-setting en vaak met studenten als proefpersonen. Soms

worden zelfs effecten gevonden die repliceren. Ondertussen schreef ik een proefschrift vol schreef op basis van één klinische trial met echte patiënten. Hoewel de context van onze onderzoeken vaak ver uit elkaar lag, heb ik veel gehad aan de soms verassende en vernieuwende interpretaties van resultaten en nuttige tips om nog eens opnieuw naar de data te kijken. Gelijkgestemden zocht ik daarom maar wat vaker op bij congressen en summer schools. In Miami, Venetië, Sydney, St.Louis, Londen, Heidelberg, Vancouver, Boston, Lyon en Pittsburgh. Het was fijn altijd weer met nieuwe ideeën en positieve feedback terug te keren. Mocht onderwijl iemand nog advies willen over hoe je optimaal een reisbudget kan besteden, welke vliegvelden fijn zijn om over te stappen of welke congreslocaties aan te bevelen zijn, dan weet je me te vinden.

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Maarten Cuypers was born on July 28, 1984 in Eindhoven, The Netherlands. He completed secondary education at the Bisschop Bekkerscollege in Eindhoven in 2001 (cum laude), and subsequently obtained his Bachelor´s degree at the Fontys University of Applied Sciences in Eindhoven in 2005. He completed the Master programs in Marketing Management (2009) and Social Psychology (Economic Psychology track, 2012) at Tilburg University. He wrote his first Master´s thesis on the patient evaluations of the care provided by the (out-of-office) general practice centers in Brabant, and his second Master´s thesis focused on medical decisions when facing health risks. After graduating, he worked for one year as a researcher at Bernhoven hospital in Uden before starting his PhD research at Tilburg University in 2013. His research focused on implementation and evaluations by patients and care providers about a patient decision aid to support treatment choice in early prostate cancer, and was conducted in close cooperation with the Elisabeth-Tweesteden hospital in Tilburg.

During his PhD project he obtained his University Teaching Qualification and Good Clinical Practice certification. Currently, he is working as a postdoctoral researcher at the department of Primary and Community care of the Radboud university medical center in Nijmegen.